

10/706,328

5/3/2007

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:33:03 ON 03 MAY 2007

=> file registry

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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0.21

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STRUCTURE FILE UPDATES: 2 MAY 2007 HIGHEST RN 934214-84-3

DICTIONARY FILE UPDATES: 2 MAY 2007 HIGHEST RN 934214-84-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

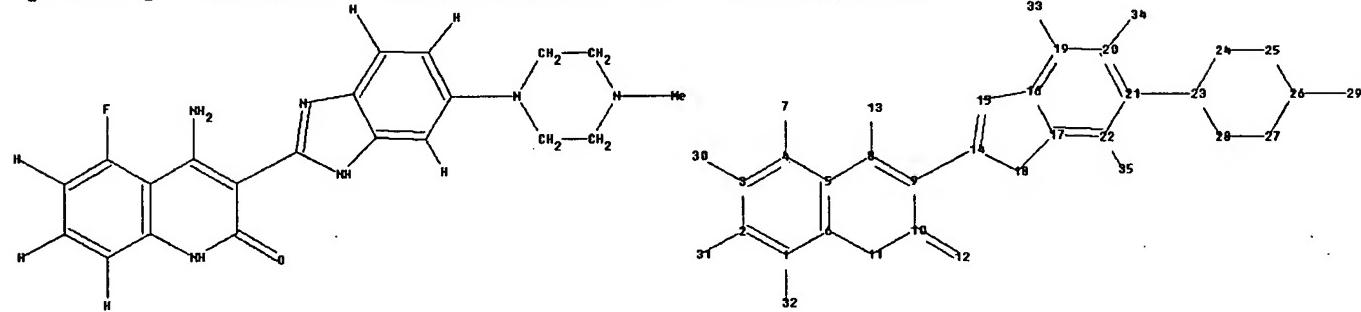
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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10706328_updated.str



chain nodes :

7 12 13 29 30 31 32 33 34 35

ring nodes :

1 2 3 4 5 6 8 9 10 11 14 15 16 17 18 19 20 21 22 23 24 25 26
27 28

chain bonds :

1-32 2-31 3-30 4-7 8-13 9-14 10-12 19-33 20-34 21-23 22-35 26-29

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-8 6-11 8-9 9-10 10-11 14-15 14-18 15-16 16-17

16-19 17-18 17-22 19-20 20-21 21-22 23-24 23-28 24-25 25-26 26-27 27-28

exact/norm bonds :

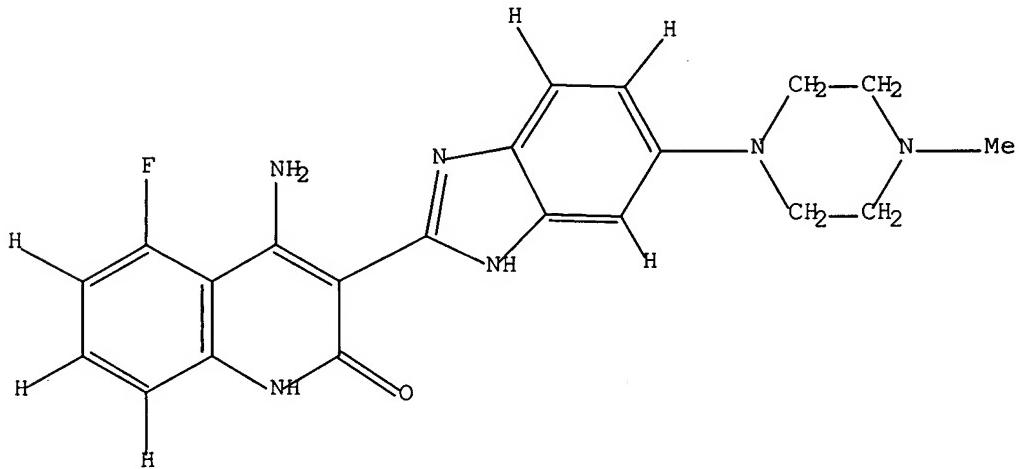
5-8 6-11 8-9 8-13 9-10 10-11 10-12 14-15 14-18 15-16 17-18 21-23 23-24
 23-28 24-25 25-26 26-27 27-28
 exact bonds :
 1-32 2-31 3-30 4-7 9-14 19-33 20-34 22-35 26-29
 normalized bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-19 17-22 19-20 20-21 21-22

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom
 11:Atom 12:CLASS 13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
 20:Atom 21:Atom
 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:CLASS 30:CLASS
 31:CLASS 32:CLASS
 33:CLASS 34:CLASS 35:CLASS

L1 STRUCTURE UPLOADED

=> d 11
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11 exa
SAMPLE SEARCH INITIATED 11:33:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 7 TO ITERATE

100.0% PROCESSED 7 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 7 TO 298
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA EXA SAM L1

=> s 11 exa full
FULL SEARCH INITIATED 11:33:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 212 TO ITERATE

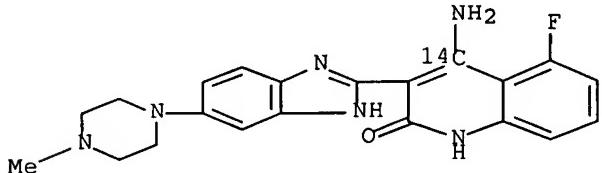
100.0% PROCESSED 212 ITERATIONS
SEARCH TIME: 00.00.01

2 ANSWERS

L3 2 SEA EXA FUL L1

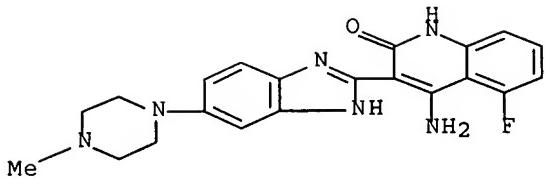
=> d 13 1-2

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN
RN 692737-81-8 REGISTRY
ED Entered STN: 14 Jun 2004
CN 2(1H)-Quinolinone-4-14C, 4-amino-5-fluoro-3-[5-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)
MF C21 H21 F N6 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN
RN 405169-16-6 REGISTRY
ED Entered STN: 12 Apr 2002
CN 2(1H)-Quinolinone, 4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2(1H)-Quinolinone, 4-amino-5-fluoro-3-[5-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]- (9CI)
OTHER NAMES:
CN 4-Amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one
CN CHIR 258
DR 804551-71-1
MF C21 H21 F N6 O
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR,
SYNTHLINE, TOXCENTER, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

30 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
30 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file medline caplus wpids uspatfull

| COST IN U.S. DOLLARS | SINCE FILE
ENTRY | TOTAL
SESSION |
|----------------------|---------------------|------------------|
| FULL ESTIMATED COST | 62.60 | 62.81 |

FILE 'MEDLINE' ENTERED AT 11:34:23 ON 03 MAY 2007

FILE 'CAPLUS' ENTERED AT 11:34:23 ON 03 MAY 2007
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FILE 'WPIDS' ENTERED AT 11:34:23 ON 03 MAY 2007
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FILE 'USPATFULL' ENTERED AT 11:34:23 ON 03 MAY 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> S 13
SAMPLE SEARCH INITIATED 11:34:29 FILE 'WPIDS'
SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00:00:01

| | | |
|------------------------|--------|--------------|
| FULL FILE PROJECTIONS: | ONLINE | **COMPLETE** |
| | BATCH | **COMPLETE** |
| PROJECTED ITERATIONS: | 0 TO | 0 |
| PROJECTED ANSWERS: | 0 TO | 0 |

L4 50 L3

=> d 14 1-50 ibib abs

L4 ANSWER 1 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:150229 CAPLUS Full-text
DOCUMENT NUMBER: 146:221063
TITLE: Method for assaying anti-tumor effect of angiogenesis inhibitor
INVENTOR(S): Uenaka, Toshimitsu; Yamamoto, Yuji; Matsui, Junji
PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 147pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| WO 2007015578 | A1 | 20070208 | WO 2006-JP315698 | 20060802 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HN, HR, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU,
SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.: JP 2005-224173 A 20050802
JP 2006-164700 A 20060614

OTHER SOURCE(S): MARPAT 146:221063

AB Disclosed is a method for predicting the anti-tumor effect of an angiogenesis inhibitor. The method comprises evaluating the EGF-dependence property of an angiogenesis inhibitor with respect to proliferation and/or survival of tumor cells, and using the evaluated EGF-dependence property as a measure. The anti-tumor effect of an angiogenesis inhibitor correlates with the EGF-dependency property of the inhibitor with respect to proliferation and/or survival of tumor cells. Therefore, an angiogenesis inhibitor is capable of exerting an excellent anti-tumor effect by using it in combination with a substance having an EGF inhibitory effect.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:144036 CAPLUS Full-text

DOCUMENT NUMBER: 146:221062

TITLE: Method for predicting antitumor efficacy of angiogenesis inhibitor

INVENTOR(S): Matsui, Junji; Semba, Taro

PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 104pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| WO 2007015569 | A1 | 20070208 | WO 2006-JP315563 | 20060801 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HN, HR, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU,
SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, | | | | |

US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-223440 A 20050801

OTHER SOURCE(S): MARPAT 146:221062

AB A method for predicting the antitumor efficacy of an angiogenesis inhibitor is provided, which comprises measuring the number of blood vessels surrounded by pericytes in tumor, and using the measurement value as a measure for the anti-tumor effect.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:119480 CAPLUS Full-text

DOCUMENT NUMBER: 146:206220

TITLE: Multicyclic sulfonamide compounds as inhibitors of histone deacetylase for the treatment of disease and their preparation

INVENTOR(S): Malecha, James W.; Noble, Stewart A.; Wiley, Brandon M.; Hoffman, Timothy Z.; Bonnefous, Celine; Sertic, Michael; Wash, Paul L.; Smith, Nicholas D.; Hassig, Christian A.; Scranton, Shawn A.; Payne, Joseph E.; Hager, Jeffery

PATENT ASSIGNEE(S): Kalypsys, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 44pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

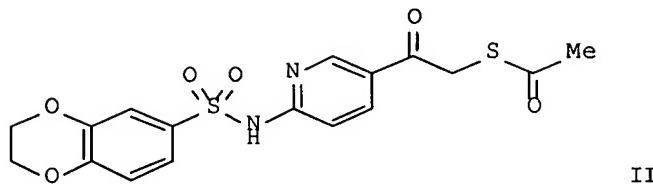
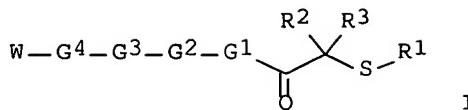
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2007027184 | A1 | 20070201 | US 2006-496784 | 20060727 |
| WO 2007016354 | A1 | 20070208 | WO 2006-US29438 | 20060727 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BR, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU,
SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.: US 2005-704091P P 20050729
US 2006-780129P P 20060307

OTHER SOURCE(S): MARPAT 146:206220

GI



AB Disclosed herein are sulfonamide compds. of formula I as described herein. Compds. of formula I wherein G1 is bond, alkenyl, alkoxy, alkoxyalkyl, alkyl, alkylamino, alkylcarbonyl, etc.; G2 is (un)substituted (mono/poly) heteroaryl; G3 is SO₂NH and derivs., NHSO₂ and derivs., C1-3 alkyl-SO₂NH and derivs., and NHSO₂-C1-3 alkyl and derivs.; G4 is bicyclic (hetero)aryl, and (hetero)cycloalkyl-fused monocyclic (hetero)aryl; W is OH and derivs., (un)substituted oxyalkyl, SH and derivs., etc.; R1 is H, PO₃H₂ and derivs., CN, (un)substituted acyl, (hetero)aryl, alkyl, aroyl, etc.; R2 and R3 are independently H, Me, and Et; and their therapeutically acceptable salts, esters, and prodrugs thereof, are claimed. Methods and compns. are disclosed for treating disease states including, but not limited to cancers, autoimmune diseases, tissue damage, central nervous system disorders, neurodegenerative disorders, fibrosis, bone disorders, polyglutamine-repeat disorders, anemias, thalassemias, inflammatory conditions, cardiovascular conditions, and disorders in which angiogenesis play a role in pathogenesis, using the compds. of the invention. In addition, methods of modulating the activity of histone deacetylase (HDAC) are also disclosed. Example compound II was prepared by chlorination of 6-chloronicotinic acid; the resulting 6-chloronicotinoyl chloride underwent alkylation of di-Me malonate to give di-Me 2-(6-chloronicotinoyl)malonate, which underwent decarboxylation to give 2-chloro-5-acetylpyridine, which underwent amination to give 2-amino-5-acetylpyridine, which underwent sulfamidation with 2,3-dihydrobenzo[1,4]dioxin-6-sulfonyl chloride to give 2,3-dihydrobenzo[1,4]dioxin-6-sulfonic acid (5-acetylpyridin-2-yl)amide, which underwent bromination to give 2,3-dihydrobenzo[1,4]dioxin-6-sulfonic acid (5-(bromoacetyl)pyridin-2-yl)amide, which underwent substitution with potassium thioacetate to give compound II. All the invention compds. were evaluated for their HDAC inhibitory activity. From the assay, it was determined that compound II exhibited in vitro and cellular IC₅₀ values of ≤ 1 μM.

L4 ANSWER 4 OF 50 , CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1252191 CAPLUS Full-text

DOCUMENT NUMBER: 146:13206

TITLE: Crystalline forms of 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one lactic acid salts

INVENTOR(S): Okhamafe, Augustus; Chou, Joyce; Gullapalli, Rampurna; Harwood, Eric; Ryckman, David; Zhu, Shuguang; Shang, Xiao

PATENT ASSIGNEE(S): Novartis A.-G., USA

SOURCE: PCT Int. Appl., 107pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2006127926 | A2 | 20061130 | WO 2006-US20296 | 20060523 |
| WO 2006127926 | A3 | 20070118 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.: US 2005-683999P P 20050523
 AB The present invention relates to non-hydrate crystalline forms of 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one lactic acid salts (I), solid pharmaceutical formulations containing the same and methods of use. The present invention also relates to crystalline hydrates of I, pharmaceutical formulations containing them and methods of use related thereto. The present invention further relates to crystalline solvates of I. I was prepared in a series of steps from 5-chloro-2-nitroaniline and 1-methylpiperazine. The crystal form of I was prepared

L4 ANSWER 5 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:1225966 CAPLUS Full-text
 DOCUMENT NUMBER: 146:722
 TITLE: Methods for treating drug resistant cancer
 INVENTOR(S): Michelson, Glenn C.; Chan, Vivien W.; Heise, Carla C.; Wiesmann, Marion; Dawes, Timothy D.
 PATENT ASSIGNEE(S): Novartis AG, USA
 SOURCE: PCT Int. Appl., 151pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2006124413 | A2 | 20061123 | WO 2006-US17922 | 20060510 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, | | | | |

KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2005-680722P

P 20050513

OTHER SOURCE(S): MARPAT 146:722

AB This invention pertains generally to methods of treating cancer. More specifically, the invention pertains to methods and 4-amino substituted quinolinone benzimidazolyl compds. such as 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one compds. and pharmaceutical formulations comprising such compds. for treating drug-resistant cancer and patients with drug resistant cancer.

L4 ANSWER 6 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1225007 CAPLUS Full-text

DOCUMENT NUMBER: 145:505480

TITLE: Process for preparation of 5-(4-methylpiperazin-1-yl)-2-nitroaniline from 1-methylpiperazine and 5-halo-2-nitroaniline.

INVENTOR(S): Calvin, Gabriel; Harwood, Eric; Ryckman, David; Zhu, Shuguang

PATENT ASSIGNEE(S): Novartis AG, USA

SOURCE: PCT Int. Appl., 88pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2006125130 | A1 | 20061123 | WO 2006-US19349 | 20060517 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.: US 2005-681893P P 20050517

OTHER SOURCE(S): CASREACT 145:505480

AB A method for synthesizing 5-(4-methylpiperazin-1-yl)-2-nitroaniline (I) comprises reaction of 1-methylpiperazine with 5-halo-2-nitroaniline at 90-110° in a first (organic) solvent followed by cooling the mixture to 85-95°, adding a second solvent, and forming a slurry of the title compound. Thus, 5-chloro-2-nitroaniline and 1-methylpiperazine were heated in EtOH at 97° for approx. 40 h; the mixture was cooled to 80° followed by addition of H2O and cooling over 4 h to room temperature to give after filtration and drying 99% I.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:816356 CAPLUS Full-text

DOCUMENT NUMBER: 146:265940

TITLE: CHIR-258 Is Efficacious in A Newly Developed Fibroblast Growth Factor Receptor 3-Expressing Orthotopic Multiple Myeloma Model in Mice

AUTHOR(S): Xin, Xiaohua; Abrams, Tinya J.; Hollenbach, Paul W.; Rendahl, Katherine G.; Tang, Yan; Oei, Yoko A.; Embry, Millicent G.; Swinarski, Debbie E.; Garrett, Evelyn N.; Pryer, Nancy K.; Trudel, Suzanne; Jallal, Bahija; Mendel, Dirk B.; Heise, Carla C.
 CORPORATE SOURCE: Translational Sciences, Chiron Corporation, Emeryville, CA, 94608, USA
 SOURCE: Clinical Cancer Research (2006), 12(16), 4908-4915
 CODEN: CCREF4; ISSN: 1078-0432
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
AB PURPOSE: The ectopically expressed and deregulated fibroblast growth factor receptor 3 (FGFR3) results from a t(4;14) chromosomal translocation that occurs in .apprx.15% of multiple myeloma (MM) patients and confers a particularly poor prognosis. This study assesses the antimyeloma activity of CHIR-258, a small-mol. inhibitor of multiple receptor tyrosine kinases that is currently in phase I trials, in a newly developed FGFR3-driven preclin. MM animal model. Exptl. Design: the authors developed an orthotopic MM model in mice using a luciferase-expressing human KMS-11-luc line that expresses mutant FGFR3 (Y373C). The antimyeloma activity of CHIR-258 was evaluated at doses that inhibited FGFR3 signaling in vivo in this FGFR3-driven animal model.
 RESULTS: Noninvasive bioluminescence imaging detected MM lesions in nearly all mice injected with KMS-11-luc cells, which were mainly localized in the spine, skull, and pelvis, resulting in frequent development of paralysis. Daily oral administration of CHIR-258 at doses that inhibited FGFR3 signaling in KMS-11-luc tumors in vivo resulted in a significant inhibition of KMS-11-luc tumor growth, which translated into a significant improvement in animal survival.
 CONCLUSIONS: the authors' data provide a relevant preclin. basis for clin. trials of CHIR-258 in FGFR3-pos. MM patients.
 REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:763835 CAPLUS Full-text
 DOCUMENT NUMBER: 145:202872
 TITLE: Treatment of metastasized tumors
 INVENTOR(S): Lopes De Menezes, Daniel; Heise, Carla; Xin, Xiaohua
 PATENT ASSIGNEE(S): Chiron Corporation, USA
 SOURCE: PCT Int. Appl., 101pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2006081445 | A2 | 20060803 | WO 2006-US2979 | 20060127 |
| WO 2006081445 | A3 | 20070111 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, | | | |

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 US 2006183750 A1 20060817 US 2006-342257 20060127
 PRIORITY APPLN. INFO.: US 2005-647568P P 20050127
 US 2005-669245P P 20050406
 US 2005-722053P P 20050929

COMPOUND TO
 TREAT METASTASIZED
 TUMORS
 no ANC or
 Cmax

OTHER SOURCE(S): MARPAT 145:202872

AB Methods of treating metastatic cancer such as metastasized tumors include administering a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt or the tautomer, or a mixture thereof to a subject. The compound, tautomer, salt of the compound, salt of the tautomer, or mixture thereof may be used to prepare medicaments for treating metastatic cancer. The variable A has the values defined herein.

L4 ANSWER 9 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:394720 CAPLUS Full-text

DOCUMENT NUMBER: 145:39944

TITLE: Inhibition of phosphorylation of the colony-stimulating factor-1 receptor (c-Fms) tyrosine kinase in transfected cells by ABT-869 and other tyrosine kinase inhibitors

AUTHOR(S): Guo, Jun; Marcotte, Patrick A.; McCall, J. Owen; Dai, Yujia; Pease, Lori J.; Michaelides, Michael R.; Davidsen, Steven K.; Glaser, Keith B.

CORPORATE SOURCE: Cancer Discovery Research (R47J), Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, USA

SOURCE: Molecular Cancer Therapeutics (2006), 5(4), 1007-1013

CODEN: MCTOCF; ISSN: 1535-7163

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The properties of several multitargeted receptor tyrosine kinase inhibitors were studied for their inhibition of colony-stimulating factor-1 receptor (CSF-1R) signaling. A structurally novel, multitargeted tyrosine kinase inhibitor (ABT-869), imatinib (ST1571), and 4 compds. currently in clin. development (AG013736, BAY 43-9006, CHIR258, and SU11248) were tested for inhibition of CSF-1R signaling in both the enzymic and cellular assays. ABT-869 showed potent CSF-1R inhibition in both the enzyme and cell-based assays (IC_{50} s < 20 nmol/L). In contrast to a previous report, we have found that imatinib has activity against human CSF-1R in both assays at submicromolar concns. In enzyme assays, we have found that the inhibition of CSF-1R by both ABT-869 and imatinib are competitive with ATP, with K_i values of 3 and 120 nmol/L, resp. SU11248 is a potent inhibitor of CSF-1R in the enzyme assay (IC_{50} = 7 nmol/L) and inhibits receptor phosphorylation in the cellular assay (IC_{50} = 61 nmol/L). AG013736 was also a potent inhibitor of CSF-1R in both assays (enzyme, IC_{50} = 16 nmol/L; cellular, IC_{50} = 21 nmol/L), whereas BAY 43-9006 is less potent in the enzyme assay (IC_{50} = 107 nmol/L) than in the cellular system (IC_{50} = 20 nmol/L). In contrast, we found that CHIR258 had less activity in the cellular assay (IC_{50} = 535 nmol/L) relative to its enzymic potency (IC_{50} = 26 nmol/L). These results show the use of a cell-based assay to confirm the inhibitory activity of lead compds. and drug candidates, such as ABT-869, against the CSF-1R protein *in situ*.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:317747 CAPLUS Full-text

DOCUMENT NUMBER: 145:305178
TITLE: Advances in oral therapy for multiple myeloma
AUTHOR(S): Morgan, Gareth J.; Krishnan, Biju; Jenner, Matthew;
Davies, Faith E.
CORPORATE SOURCE: Royal Marsden Hospital and Institute of Cancer
Research, London, UK
SOURCE: Lancet Oncology (2006), 7(4), 316-325
CODEN: LOANBN; ISSN: 1470-2045
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Conventional i.v. chemotherapy regimens are toxic, cumbersome, and neg. affect patients' quality of life, with oral treatment preferable to most patients with cancer. Multiple myeloma is the second most common haematol. malignant disease, but cannot be cured with conventional and high-dose chemotherapy. New oral treatments that target myeloma cells or bone marrow are being developed that are highly effective yet have low toxic effects, such as the immunomodulatory drugs thalidomide and lenalidomide. Several treatments in early development have shown antimyeloma activity, including: CHIR-258, which inhibits fibroblast growth factor receptor 3; NVP-ADW742, which inhibits insulin-like growth factor receptor 1; and PTK787, which inhibits vascular endothelial growth factor. Addnl. drugs aimed at switching off silenced genes include histone deacetylase inhibitors. The availability of these various oral treatments is hoped to improve regimens that, if used sequentially or in combination, offer the potential of making multiple myeloma a chronic disease, thereby extending patients' lifespans and improving quality of life.

REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:268466 CAPLUS Full-text
DOCUMENT NUMBER: 144:324798
TITLE: Simultaneous use of sulfonamide-containing compound and angiogenesis inhibitor
INVENTOR(S): Owa, Takashi; Ozawa, Yoichi; Semba, Taro
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 270 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|----------|
| WO 2006030941 | A1 | 20060323 | WO 2005-JP17228 | 20050913 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | 20060323 | WO 2005-JP17238 | 20050913 |
| WO 2006030947 | A1 | 20060323 | WO 2005-JP17228 | 20050913 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM

US 2006135486 A1 20060622 US 2005-226655 20050913

PRIORITY APPLN. INFO.: US 2004-609452P P 20040913
JP 2005-54150 A 20050228
JP 2005-54475 A 20050228

OTHER SOURCE(S): MARPAT 144:324798

AB A pharmaceutical composition comprising a sulfonamide-containing compound combined with an angiogenesis inhibitor.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:167710 CAPLUS Full-text

DOCUMENT NUMBER: 144:267266

TITLE: Flt3 inhibitors for immune suppression

INVENTOR(S): Small, Donald; Whartenby, Katherine A.; Pardoll, Drew

PATENT ASSIGNEE(S): The Johns Hopkins University, USA

SOURCE: PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|------------|
| WO 2006020145 | A2 | 20060223 | WO 2005-US25318 | 20050714 |
| WO 2006020145 | A3 | 20070308 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | |
| AU 2005274852 | A1 | 20060223 | AU 2005-274852 | 20050714 |
| CA 2574150 | A1 | 20060223 | CA 2005-2574150 | 20050714 |
| EP 1778224 | A2 | 20070502 | EP 2005-790718 | 20050714 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
BA, HR, MK, YU | | | | |
| PRIORITY APPLN. INFO.: | | | US 2004-589511P | P 20040719 |
| | | | WO 2005-US25318 | W 20050714 |
| OTHER SOURCE(S): | MARPAT 144:267266 | | | |

AB New methods are provided for suppressing the immune system and for treating immune related disorders. Therapies of the invention include administration of an FLT3 inhibitor compound to a subject in need thereof, such as a subject suffering from organ rejection, bone marrow transplant rejection, acquired immune deficiency syndrome, arthritis, aplastic anemia, graft-vs.-host disease, Graves' disease, established exptl. allergic encephalomyelitis, multiple sclerosis, lupus, or a neurol. disorder. Methods are also provided for screening therapeutic agents for treating immune disorders, including the use of a mouse having an elevated level of FLT3 receptor activity.

L4 ANSWER 13 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1341902 CAPLUS Full-text

DOCUMENT NUMBER: 144:232902

TITLE: LHMDS mediated tandem acylation-cyclization of 2-aminobenzenecarbonitriles with 2-benzimidazol-2-yl acetates: a short and efficient route to the synthesis of 4-amino-3-benzimidazol-2-ylhydroquinolin-2-ones
Antonios-McCrea, William R.; Frazier, Kelly A.; Jazan, Elisa M.; Machajewski, Timothy D.; McBride, Christopher M.; Pecchi, Sabina; Renhowe, Paul A.; Shafer, Cynthia M.; Taylor, Clarke

AUTHOR(S): Antonios-McCrea, William R.; Frazier, Kelly A.; Jazan, Elisa M.; Machajewski, Timothy D.; McBride, Christopher M.; Pecchi, Sabina; Renhowe, Paul A.; Shafer, Cynthia M.; Taylor, Clarke
CORPORATE SOURCE: Small Molecule Drug Discovery, Medicinal Chemistry Department, Chiron Corporation, Emeryville, CA, 94608, USA

SOURCE: Tetrahedron Letters (2006), 47(5), 657-660
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:232902

AB The discovery of a mild, one-pot tandem acylation-cyclization for the synthesis of 4-amino-3-(2-benzimidazolyl)quinolinone derivs. from 2-aminobenzonitrile derivs. and Et (2-benzimidazolyl)acetate derivs. is described. Among the reagents evaluated, lithium hexamethyldisilazide (LHMDS) was the most efficient.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1242789 CAPLUS Full-text

DOCUMENT NUMBER: 143:477969

TITLE: Preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma

INVENTOR(S): Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla C.; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Wiesmann, Marion; Zhu, Shuguang
Chiron Corporation, USA

PATENT ASSIGNEE(S): U.S. Pat. Appl. Publ., 239 pp., Cont.-in-part of U.S. Ser. No. 644,055.

SOURCE: CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

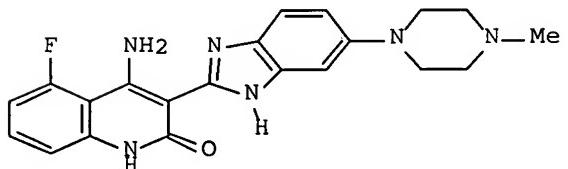
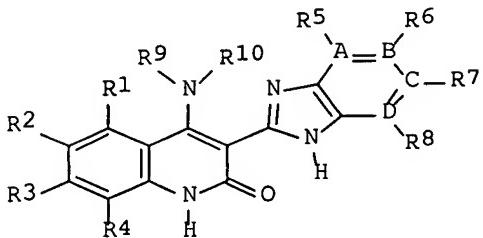
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2005261307 | A1 | 20051124 | US 2004-983174 | 20041105 |
| US 2004092535 | A1 | 20040513 | US 2003-644055 | 20030819 |

Compound to TREAT
MULTIPLE MYELOMA
NO ANC or
Cmax

METHOD OF INHIBITING
TROPOLE KINASE no ANC
or Cmax

| | | | | |
|------------------------|----|----------|-----------------|-------------|
| CN 1692112 | A | 20051102 | CN 2003-824565 | 20030819 |
| US 2005203101 | A1 | 20050915 | US 2004-839793 | 20040505 |
| PRIORITY APPLN. INFO.: | | | US 2002-405729P | P 20020823 |
| | | | US 2002-426107P | P 20021113 |
| | | | US 2002-426226P | P 20021113 |
| | | | US 2002-426282P | P 20021113 |
| | | | US 2002-428210P | P 20021121 |
| | | | US 2003-460327P | P 20030403 |
| | | | US 2003-460328P | P 20030403 |
| | | | US 2003-460493P | P 20030403 |
| | | | US 2003-478916P | P 20030616 |
| | | | US 2003-484048P | P 20030701 |
| | | | US 2003-644055 | A2 20030819 |
| | | | US 2003-517915P | P 20031107 |
| | | | US 2003-526425P | P 20031202 |
| | | | US 2003-526426P | P 20031202 |
| | | | US 2004-546017P | P 20040219 |

OTHER SOURCE(S) : MARPAT 143:477969
GI



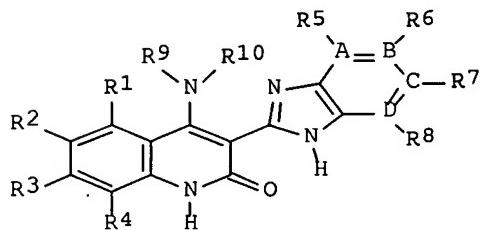
AB The title compds. I [A, B, C, and D = C, N; R1-R3 = H, halo, CN, NO₂, etc.; R4 = H, alkyl; R5-R8 = H, halo, CN, NO₂, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H], useful for inhibiting fibroblast growth factor receptor 3 or treating a biol. condition mediated by fibroblast growth factor receptor 3, were prepared. E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one (II), starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The majority of the exemplary compds. I displayed an IC₅₀ of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC₅₀ values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ with IC₅₀ values of less than 1 μM. The mentioned above compound II was tested in various tests and showed significant antiproliferative activity. II inhibited

FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

L4 ANSWER 15 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:1223876 CAPLUS Full-text
 DOCUMENT NUMBER: 143:477966
 TITLE: Preparation of benzimidazole quinolinones for inhibiting a checkpoint kinase 1 and their use in combination therapy for cancer
 INVENTOR(S): Gesner, Thomas G.; Barsanti, Paul A.; Harrison, Stephen D.; Ni, Zhi-Jie; Brammeier, Nathan M.; Zhou, Yasheen; Le, Vincent P.
 PATENT ASSIGNEE(S): Chiron Corporation, USA
 SOURCE: U.S. Pat. Appl. Publ., 249 pp., Cont.-in-part of U.S. Ser. No. 644,055.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|-----------------|-----------------|----------|
| US 2005256157 | A1 | 20051117 | US 2005-41191 | 20050121 |
| US 2004092535 | A1 | 20040513 | US 2003-644055 | 20030819 |
| CN 1692112 | A | 20051102 | CN 2003-824565 | 20030819 |
| US 2005203101 | A1 | 20050915 | US 2004-839793 | 20040505 |
| PRIORITY APPLN. INFO.: | | | | |
| | | US 2002-405729P | P | 20020823 |
| | | US 2002-426107P | P | 20021113 |
| | | US 2002-426226P | P | 20021113 |
| | | US 2002-426282P | P | 20021113 |
| | | US 2002-428210P | P | 20021121 |
| | | US 2003-460327P | P | 20030403 |
| | | US 2003-460328P | P | 20030403 |
| | | US 2003-460493P | P | 20030403 |
| | | US 2003-478916P | P | 20030616 |
| | | US 2003-484048P | P | 20030701 |
| | | US 2003-644055 | A2 | 20030819 |
| | | US 2004-538984P | P | 20040123 |

OTHER SOURCE(S): CASREACT 143:477966; MARPAT 143:477966
 GI



AB The title compds. [I; A, B, C, D = C, N; R1 = H, halo, CN, NO₂, etc.; R2, R3 = H, halo, NO₂, CN, etc.; R4 = H, (un)substituted alkyl; R5, R8 = H, (un)substituted alkyl, alkenyl, heterocyclyl; or R5 may be absent if A = N; or R8 may be absent if D = N; R6, R7 = H, halo, NO₂, CN, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H; or R9 and R10 join together to form one or more rings, each having 5-7 members], useful for inhibiting checkpoint kinase 1, inducing cell cycle progression, and increasing apoptosis in cells, were prepared. E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The compds. I were tested against various kinases. Two of the prepared compds. I, 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloroquinolin-2-(1H)-one and 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(piperidin-2-ylmethyl)amino]quinolin-2(1H)-one, were found to be potent inhibitors of CHK1 with IC₅₀ of 0.32 nM and 0.63 nM, resp. The majority of the exemplary compds. I displayed an IC₅₀ of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC₅₀ values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC₅₀ values of less than 1 μM. The compds. I may be used to prepare pharmaceutical compns. and may be used in conjunction with DNA damaging agents.

L4 ANSWER 16 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:976928 CAPLUS Full-text

DOCUMENT NUMBER: 143:279443

TITLE: 4-Amino-3-(benzimidazol-2-yl)quinolin-2-one derivatives for the modulation of inflammatory and metastatic processes

INVENTOR(S): Lee, Sang H.; Heise, Carla C.

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 145 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

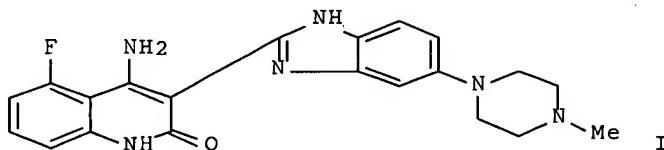
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2005082340 | A2 | 20050909 | WO 2005-US5316 | 20050218 |
| WO 2005082340 | A3 | 20060504 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG | | | | |
| AU 2005216904 | A1 | 20050909 | AU 2005-216904 | 20050218 |
| CA 2556872 | A1 | 20050909 | CA 2005-2556872 | 20050218 |
| US 2005239825 | A1 | 20051027 | US 2005-61386 | 20050218 |

EP 1718306 A2 20061108 EP 2005-723338 20050218
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,
 BA, HR, IS, YU
 PRIORITY APPLN. INFO.: US 2004-546395P P 20040220
 US 2004-547103P P 20040223
 US 2004-554771P P 20040319
 WO 2005-US5316 W 20050218

OTHER SOURCE(S) : MARPAT 143:279443
 GI



AB The invention provides methods for using of using 4-Amino-3-(benzimidazol- 2-yl)quinolin-2-one derivs. (Markush included), or a salt or tautomer thereof, in the treatment of disorders relating to cell adhesion and metastatic processes. Preparation of I is included.

L4 ANSWER 17 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:696750 CAPLUS Full-text

DOCUMENT NUMBER: 143:166661

~~TITLE:~~ Use of PDGF receptor tyrosine kinase (PDGF-R TK) inhibitors for the treatment of myocarditis and its complications

~~INVENTOR(S):~~ Leipner, Carola; Boehmer, Frank-Dietmar; Gruen, Katja; Shetty, Suraj Shivappa; Massimini, Giorgio

~~PATENT ASSIGNEE(S):~~ Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

~~SOURCE:~~ PCT Int. Appl., 19 pp.

~~CODEN:~~ PIXXD2

~~DOCUMENT TYPE:~~ Patent

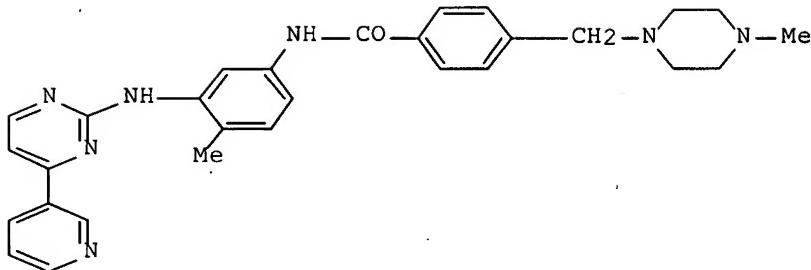
~~LANGUAGE:~~ English

~~FAMILY ACC. NUM. COUNT:~~ 1

~~PATENT INFORMATION:~~

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2005070432 | A1 | 20050804 | WO 2005-EP749 | 20050126 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: GB 2004-1761 A 20040127
 GI



I

AB The invention discloses the use of a PDGF-R TK inhibitor, e.g. I, or a pharmaceutically acceptable salt thereof, for the manufacture of pharmaceutical compns. for the treatment of myocarditis and/or its complications.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:629989 CAPLUS Full-text

DOCUMENT NUMBER: 143:452249

TITLE: CHIR-258: A Potent Inhibitor of FLT3 Kinase in Experimental Tumor Xenograft Models of Human Acute Myelogenous Leukemia

AUTHOR(S): Lopes de Menezes, Daniel E.; Peng, Jing; Garrett, Evelyn N.; Louie, Sharianne G.; Lee, Sang H.; Wiesmann, Marion; Tang, Yan; Shephard, Lee; Goldbeck, Cheryl; Oei, Yoko; Ye, Helen; Aukerman, Sharon L.; Heise, Carla

CORPORATE SOURCE: Biopharma Research and Development, Chiron Corp., Emeryville, CA, USA

SOURCE: Clinical Cancer Research (2005), 11(14), 5281-5291
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: Fms-like tyrosine kinase 3 (FLT3) encodes a receptor tyrosine kinase (RTK) for which activating mutations have been identified in a proportion of acute myelogenous leukemia (AML) patients and associated with poor clin. prognosis. Given the relevance of FLT3 mutations in AML, we investigated the activity of CHIR-258, an orally active, multitargeted small mol., with potent activity against FLT3 kinase and class III, IV, and V RTKs involved in endothelial and tumor cell proliferation in AML models. Exptl. Design: CHIR-258 was tested on two human leukemic cell lines in vitro and in vivo with differing FLT3 mutational status [MV4;11 cells express FLT3 internal tandem duplications (ITD) vs. RS4;11 cells with wild-type (WT) FLT3]. Results: Antiproliferative activity of CHIR-258 against MV4;11 was .apprx.24-fold greater compared with RS4;11, indicating more potent inhibition against cells with constitutively activated FLT3 ITD. Dose-dependent down modulation of receptor phosphorylation and downstream signaling [signal transducer and activator of transcription 5 (STAT5) and extracellular signal-regulated kinase (ERK)/mitogen-activated protein kinase] in MV4;11 cells with CHIR-258 confirmed the mol. mechanism of action. Target modulation of phospho-FLT3, phospho-STAT5, and phospho-ERK in MV4;11 tumors was achieved at biol. active

doses of CHIR-258. Tumor regressions and eradication of AML cells from the bone marrow were shown in s.c. and bone marrow engraftment leukemic xenograft models. Tumor responses were characterized by decreased cellular proliferation and pos. immunohistochem. staining for active caspase-3 and cleaved poly(ADP-ribose) polymerase, suggesting cell death was mediated in part via apoptosis. Conclusions: These data indicate that CHIR-258 may be an effective therapy in FLT3-associated AML and warrants clin. trials.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

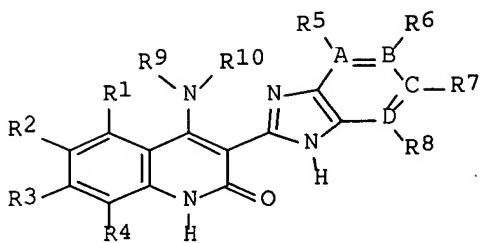
L4 ANSWER 19 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:451351 CAPLUS Full-text
 DOCUMENT NUMBER: 143:7710
 TITLE: Preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma
 INVENTOR(S): Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla C.; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Wiesmann, Marion; Zhu, Shuguang
 PATENT ASSIGNEE(S): Chiron Corporation, USA
 SOURCE: PCT Int. Appl., 567 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2005047244 | A2 | 20050526 | WO 2004-US36956 | 20041105 |
| WO 2005047244 | A3 | 20061221 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004289672 | A1 | 20050526 | AU 2004-289672 | 20041105 |
| CA 2544186 | A1 | 20050526 | CA 2004-2544186 | 20041105 |
| US 2005137399 | A1 | 20050623 | US 2004-982757 | 20041105 |
| US 2005209247 | A1 | 20050922 | US 2004-982543 | 20041105 |
| EP 1692085 | A2 | 20060823 | EP 2004-810419 | 20041105 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU | | | | |
| JP 2007510665 | T | 20070426 | JP 2006-538512 | 20041105 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 2003-517915P | P 20031107 |
| | | | US 2003-526425P | P 20031202 |
| | | | US 2003-526426P | P 20031202 |
| | | | US 2004-546017P | P 20040219 |
| | | | WO 2004-US36956 | W 20041105 |

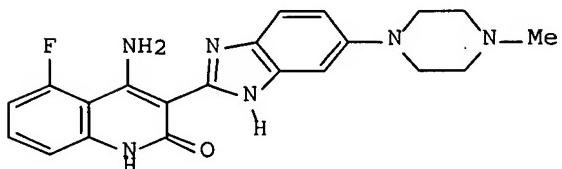
OTHER SOURCE(S): MARPAT 143:7710

GI

SYNTHESIS



I



II

AB The title compds. I [A, B, C, and D = C, N; R1-R3 = H, halo, CN, NO₂, etc.; R4 = H, alkyl; R5-R8 = H, halo, CN, NO₂, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H], useful for inhibiting fibroblast growth factor receptor 3 or treating a biol. condition mediated by fibroblast growth factor receptor 3, were prepared. E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one (II), starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The majority of the exemplary compds. I displayed an IC₅₀ of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC₅₀ values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC₅₀ values of less than 1 μM. The mentioned above compound II was tested in various tests and showed significant antiproliferative activity. II inhibits FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

L4 ANSWER 20 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:451119 CAPLUS Full-text

DOCUMENT NUMBER: 143:7732

TITLE: Process for preparation of benzimidazolylquinolones by reaction of aminobenzonitriles with benzimidazolylacetates.

INVENTOR(S): Cai, Shaopei; Chou, Joyce; Harwood, Eric; Ryckman, David; Shang, Xiao; Zhu, Shuguang; Machajewski, Timothy D.

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

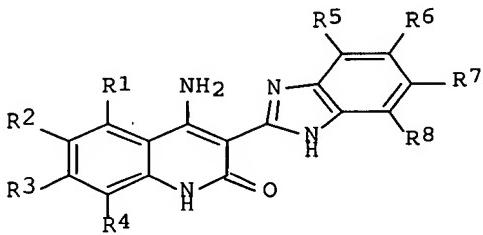
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

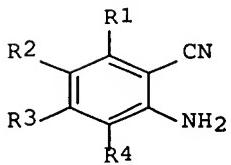
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|------------|
| WO 2005046590 | A2 | 20050526 | WO 2004-US37051 | 20041105 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG | | | | |
| AU 2004288709 | A1 | 20050526 | AU 2004-288709 | 20041105 |
| CA 2543820 | A1 | 20050526 | CA 2004-2543820 | 20041105 |
| US 2005137399 | A1 | 20050623 | US 2004-982757 | 20041105 |
| US 2005209247 | A1 | 20050922 | US 2004-982543 | 20041105 |
| EP 1682529 | A2 | 20060726 | EP 2004-810468 | 20041105 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | |
| CN 1878766 | A | 20061213 | CN 2004-80032837 | 20041105 |
| JP 2007510668 | T | 20070426 | JP 2006-538526 | 20041105 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 2003-517915P | P 20031107 |
| | | | US 2003-526425P | P 20031202 |
| | | | US 2003-526426P | P 20031202 |
| | | | US 2004-546017P | P 20040219 |
| | | | WO 2004-US37051 | W 20041105 |

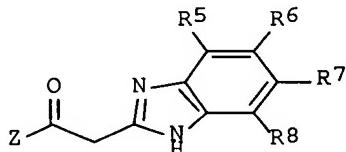
OTHER SOURCE(S) : CASREACT 143:7732; MARPAT 143:7732
GI



I



II



III

AB Title compds. [I; R1-R4 = H, Cl, Br, F, iodo, OR10, NR11R12, (substituted) alkyl, aryl, alkenyl, alkynyl, heterocyclyl, heterocyclylalkyl; R5-R8 = H, F, Cl, Br, iodo, OR13, NR14R15, SR16, (substituted) alkyl, aryl, alkenyl, alkynyl, heterocyclyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, heterocyclyloxyalkyl; R10, R13 = (substituted) alkyl, aryl, heterocyclyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, heterocyclyloxyalkyl; R11-R16 =

(substituted) alkyl, aryl, heterocyclyl], were prepared by reaction of aminobenzonitriles (II; R1-R4 as above) with benzimidazolylacetates (III; R5-R8 as above; Z = OR9a, NR9bR9c; R9a-R9c = alkyl) in the presence of the Na or K salt of a base. Thus, Et [6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]acetate (preparation given), 2-amino-6-fluorobenzonitrile, and potassium bis(trimethylsilyl)amide were stirred together in THF at 40-62° for 1 h to give 47.9% 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one.

L4 ANSWER 21 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:451118 CAPLUS Full-text

DOCUMENT NUMBER: 143:7709

TITLE: Preparation of benzimidazole quinolinones and lactate salts thereof for inhibiting vascular endothelial growth factor receptor tyrosine kinase

INVENTOR(S): Cai, Shaopei; Chou, Joyce; Harwood, Eric; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Zhu, Shuguang

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 215 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

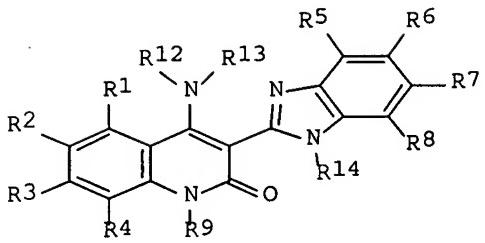
FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

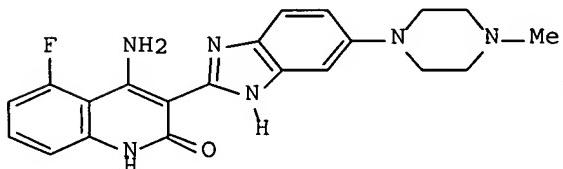
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2005046589 | A2 | 20050526 | WO 2004-US36941 | 20041105 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004288692 | A1 | 20050526 | AU 2004-288692 | 20041105 |
| CA 2544492 | A1 | 20050526 | CA 2004-2544492 | 20041105 |
| US 2005137399 | A1 | 20050623 | US 2004-982757 | 20041105 |
| US 2005209247 | A1 | 20050922 | US 2004-982543 | 20041105 |
| EP 1699421 | A2 | 20060913 | EP 2004-816941 | 20041105 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU | | | | |
| BR 2004016143 | A | 20070102 | BR 2004-16143 | 20041105 |
| PRIORITY APPLN. INFO.: | | | US 2003-517915P | P 20031107 |
| | | | US 2003-526425P | P 20031202 |
| | | | US 2003-526426P | P 20031202 |
| | | | US 2004-546017P | P 20040219 |
| | | | WO 2004-US36941 | W 20041105 |

OTHER SOURCE(S): CASREACT 143:7709; MARPAT 143:7709

GI



I



II

AB The title compds. I [R1-R4 = H, halo, CN, NO₂, etc.; R5-R8 = H, halo, NO₂, etc.; R9 = H; R12 = H, alkyl, aryl, heterocyclyl; R13 = H, alkyl, aryl, heterocyclyl, etc.; R14 = H] and their pharmaceutically acceptable lactate salts, useful for inhibiting vascular endothelial growth factor receptor tyrosine kinase, were prepared E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one (II) and its lactate salt, starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The pharmaceutically acceptable salts of I have improved aqueous solubility and desirable drug substance properties. Many of the exemplary compds. I displayed an IC₅₀ of less than 10 μM with respect to Flt-1, KDR, PDGF, c-KIT, FLT-3, VEGFR1, VEGFR2, c-Met, CSF-1, FGFR3 and/or bFGFR. In addition, many of the exemplary compds. exhibited IC₅₀ value of less than 10 μM with respect to PDGFR. The 4-amino substituted compds. I such as II were found to be potent inhibitors of various kinases such as VEGFR2 (KDR, Flk-1), FGFR1 and PDGFRβ with IC₅₀'s ranging from 10-27 nM. II inhibits FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

L4 ANSWER 22 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:418830 CAPLUS Full-text

DOCUMENT NUMBER: 143:221928

TITLE: In vivo Target Modulation and Biological Activity of CHIR-258, a Multitargeted Growth Factor Receptor Kinase Inhibitor, in Colon Cancer Models

AUTHOR(S): Lee, Sang Hoon; Lopes de Menezes, Daniel; Vora, Jayesh; Harris, Alex; Ye, Helen; Nordahl, Lara; Garrett, Evelyn; Samara, Emil; Aukerman, Sharon Lea; Gelb, Arnold B.; Heise, Carla

CORPORATE SOURCE: Departments of Pharmacology, and Experimental Pathology, Pharmacokinetics and Drug Metabolism, and Applied Biochemistry, Translational Medicine, Chiron Corp., Emeryville, CA, USA

SOURCE: Clinical Cancer Research (2005), 11(10), 3633-3641

CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: To evaluate the therapeutic and biol. effects of CHIR-258, an orally bioavailable, potent inhibitor of class III-V receptor tyrosine kinases, in colon cancer models. Exptl. Design: The pharmacol. activity of CHIR-258 was characterized by monitoring target modulation as well as by evaluating the antitumor and antiangiogenic effects in human colon xenograft models. Results: CHIR-258 inhibits vascular endothelial growth factor receptor 1/2, fibroblast growth factor receptor 1/3, and platelet-derived growth factor receptor β (PDGFR β) and shows both antitumor and antiangiogenic activities in vivo. Treatment of KM12L4a human colon cancer cells with CHIR-258 resulted in a dose-dependent inhibition of vascular endothelial growth factor receptor 1 and PDGFR β phosphorylation and reduction of phosphorylated extracellular signal-regulated kinase (ERK) levels, indicating modulation of target receptors and downstream signaling. In vivo administration of CHIR-258 resulted in significant tumor growth inhibition and tumor regressions, including large, established tumors (500-1,000 mm³). Immunohistochem. anal. showed a reduction of phosphorylated PDGFR β and phosphorylated ERK in tumor cells after oral dosing with CHIR-258 compared with control tumors. These changes were accompanied by decreased tumor cell proliferation rate and reduced intratumoral microvessel d. CHIR-258 inhibited the phosphorylation of PDGFR β and ERK phosphorylation in tumors within 2 h following dosing and the inhibitory activity was sustained for >24 h. Significant antitumor activity was observed with intermittent dosing schedules, indicating a sustained biol. activity. Conclusion: These studies provide evidence that biol. activity of CHIR-258 in tumors correlates with efficacy and aids in the identification of potential biomarkers of this multitargeted receptor tyrosine kinase inhibitor. CHIR-258 exhibits properties that make it a promising candidate for clin. development in a variety of solid and hematol. malignancies.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:369248 CAPLUS Full-text
 DOCUMENT NUMBER: 142:428777
 TITLE: Antibodies of fibroblast growth factor receptor-1 and uses as inhibitors for the treatment of obesity
 INVENTOR(S): Sun, Haijun
 PATENT ASSIGNEE(S): Imclone Systems Incorporated, USA
 SOURCE: PCT Int. Appl., 104 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2005037235 | A2 | 20050428 | WO 2004-US34970 | 20041018 |
| WO 2005037235 | A3 | 20051222 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

| | | | |
|--|-------------|-----------------|------------|
| CA 2542638 | A1 20050428 | CA 2004-2542638 | 20041018 |
| EP 1680140 | A2 20060719 | EP 2004-796034 | 20041018 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | |
| PRIORITY APPLN. INFO.: | | US 2003-512255P | P 20031016 |
| | | WO 2004-US34970 | W 20041018 |

AB The present invention is directed to an antibody or fragments thereof that are specific for a fibroblast growth factor receptor (FGFR)-1(IIIB), FGFR-1(IIIC), and/or FGFR-4. Also, provided herein, are vectors and host cells comprising the nucleic acids encoding those antibodies. The present invention further provides methods of antagonizing FGFR-1 or FGFR-4 as a treatment for obesity, diabetes, or a condition related thereto, and methods of reducing food intake.

L4 ANSWER 24 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:295572 CAPLUS Full-text

DOCUMENT NUMBER: 143:591

~~TITLE~~: CHIR-258, a novel, multitargeted tyrosine kinase inhibitor for the potential treatment of t(4;14) multiple myeloma

~~AUTHOR(S)~~: Trudel, Suzanne; Li, Zhi Hua; Wei, Ellen; Wiesmann, Marion; Chang, Hong; Chen, Christine; Reece, Donna; Heise, Carla; Stewart, A. Keith

~~CORPORATE SOURCE~~: Department of Medical Oncology, Princess Margaret Hospital and McLaughlin Centre for Molecular Medicine, University of Toronto, Toronto, ON, Can.

~~SOURCE~~: Blood (2005), 105(7), 2941-2948
CQDEN: BLOOA; ISSN: 0006-4971

~~PUBLISHER~~: American Society of Hematology

~~DOCUMENT TYPE~~: Journal

~~LANGUAGE~~: English

AB The t(4;14) translocation that occurs uniquely in a subset (15%) of patients with multiple myeloma (MM) results in the ectopic expression of the receptor Tyr kinase (RTK), fibroblast growth factor receptor 3 (FGFR3). Inhibition of activated FGFR3 in MM cells induces apoptosis, validating FGFR3 as a therapeutic target in t(4;14) MM and encouraging the clin. development of FGFR3 inhibitors for the treatment of these patients, who have a poor prognosis. The authors describe here the characterization of a novel, small-mol. inhibitor of class III, IV, and V RTKs, CHIR-258, as an inhibitor of FGFR3. CHIR-258 potently inhibits FGFR3 with an inhibitory concentration of 50% (IC50) of 5 nM in in vitro kinase assays and selectively inhibited the growth of B9 cells and human myeloma cell lines expressing wild-type (WT) or activated mutant FGFR3. In responsive cell lines, CHIR-258 induced cytostatic and cytotoxic effects. Importantly, addition of interleukin 6(IL-6) or insulin growth factor 1 (IGF-1) or coculture on stroma did not confer resistance to CHIR-258. In primary myeloma cells from t(4;14) patients, CHIR-258 inhibited downstream extracellular signal-regulated kinase (ERK) 1/2 phosphorylation with an associated cytotoxic response. Finally, therapeutic efficacy of CHIR-258 was demonstrated in a xenograft mouse model of FGFR3 MM. These studies support the clin. evaluation of CHIR-258 in MM.

~~REFERENCE COUNT~~: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:99470 CAPLUS Full-text

DOCUMENT NUMBER: 142:197889

~~TITLE~~: Fluoro substituted omega-carboxyaryl diphenyl urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases

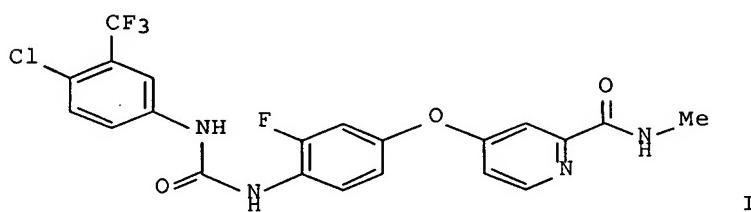
~~INVENTOR(S)~~: Dumas, Jacques; Boyer, Stephen; Riedl, Bernd; Wilhelm, ~

PATENT ASSIGNEE(S) : Scott
 Bayer Pharmaceuticals Corporation, USA
 SOURCE: PCT Int. Appl., 68 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|---|--|------------|
| WO 2005009961 | A2 | 20050203 | WO 2004-US23500 | 20040722 |
| WO 2005009961 | A3 | 20050331 | | |
| WO 2005009961 | B1 | 20050602 | | |
| | | | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SB, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG | |
| AU 2004259760 | A1 | 20050203 | AU 2004-259760 | 20040722 |
| CA 2532865 | A1 | 20050203 | CA 2004-2532865 | 20040722 |
| US 2005038080 | A1 | 20050217 | US 2004-895985 | 20040722 |
| EP 1663978 | A2 | 20060607 | EP 2004-786091 | 20040722 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | |
| BR 2004012219 | A | 20060822 | BR 2004-12219 | 20040722 |
| CN 1856469 | A | 20061101 | CN 2004-80021091 | 20040722 |
| JP 2006528196 | T | 20061214 | JP 2006-521221 | 20040722 |
| NO 2006000870 | A | 20060407 | NO 2006-870 | 20060222 |
| PRIORITY APPLN. INFO.: | | | US 2003-489102P | P 20030723 |
| | | | US 2004-540326P | P 20040202 |
| | | | WO 2004-US23500 | W 20040722 |

OTHER SOURCE(S) : CASREACT 142:197889

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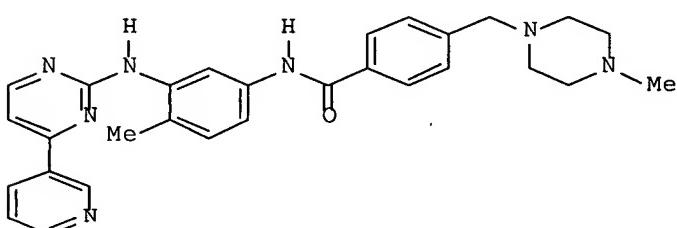


AB Title compound I is prepared and salts thereof is prepared in several steps from 3-fluoro-4-nitrophenol, 4-chloro-N-methylpyridine-2-carboxamide and 4-chloro-3-(trifluoromethyl)phenylisocyanate. I inhibits PDGFR tyrosine kinase with IC50 = 83 nM. I is useful for the treatment of, e.g., inflammation and as an antiproliferative agent.

L4 ANSWER 26 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:1059176 CAPLUS Full-text
 DOCUMENT NUMBER: 142:32986
 TITLE: Use of a c-abl-, PDGFR-, or c-kit-tyrosine kinase inhibitor for the treatment of diabetes
 INVENTOR(S): Hagerkvist, Robert Per; Welsh, Nils Richard
 PATENT ASSIGNEE(S): Swed.
 SOURCE: PCT Int. Appl., 22 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|------------|
| WO 2004105763 | A2 | 20041209 | WO 2004-EP5679 | 20040526 |
| WO 2004105763 | A3 | 20050602 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG | | | | |
| AU 2004243491 | A1 | 20041209 | AU 2004-243491 | 20040526 |
| CA 2526594 | A1 | 20041209 | CA 2004-2526594 | 20040526 |
| EP 1631291 | A2 | 20060308 | EP 2004-739375 | 20040526 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| BR 2004010704 | A | 20060613 | BR 2004-10704 | 20040526 |
| CN 1794995 | A | 20060628 | CN 2004-80014278 | 20040526 |
| JP 2006528225 | T | 20061214 | JP 2006-529925 | 20040526 |
| NO 2005006188 | A | 20051223 | NO 2005-6188 | 20051223 |
| US 2007072932 | A1 | 20070329 | US 2006-556984 | 20060622 |
| PRIORITY APPLN. INFO.: | | | GB 2003-12086 | A 20030527 |
| | | | GB 2004-2682 | A 20040206 |
| | | | WO 2004-EP5679 | W 20040526 |

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AB The invention discloses the use of a c-Abl-, PDGFR-, or c-kit-tyrosine kinase inhibitor, e.g. I, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of diabetes, including type I or type II diabetes.

L4 ANSWER 27 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:428803 CAPLUS Full-text

DOCUMENT NUMBER: 141:1211

TITLE: Methods of treating cancer with a methylpiperazinyl benzimidazolyl quinolinone and related methods

INVENTOR(S): Machajewski, Timothy D.; Hannah, Alison; Harwood, Eric; Haroldsen, Peter; Heise, Carla C.; Samara, Emil; Shang, Xiao; Vora, Jayesh; Zhu, Shuguang

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-----------------|------------------|----------|
| WO 2004043389 | A2 | 20040527 | WO 2003-US35806 | 20031112 |
| WO 2004043389 | A3 | 20040805 | | |
| WO 2004043389 | B1 | 20040916 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2501932 | A1 | 20040527 | CA 2003-2501932 | 20031112 |
| AU 2003290699 | A1 | 20040603 | AU 2003-290699 | 20031112 |
| US 2004220196 | A1 | 20041104 | US 2003-706328 | 20031112 |
| EP 1565187 | A2 | 20050824 | EP 2003-783281 | 20031112 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003016229 | A | 20051004 | BR 2003-16229 | 20031112 |
| CN 1711088 | A | 20051221 | CN 2003-80103178 | 20031112 |
| JP 2006511616 | T | 20060406 | JP 2005-507133 | 20031112 |
| IN 2005KN00793 | A | 20060303 | IN 2005-KN793 | 20050503 |
| NO 2005002760 | A | 20050720 | NO 2005-2760 | 20050607 |
| PRIORITY APPLN. INFO.: | | | | |
| | | US 2002-426107P | P | 20021113 |
| | | US 2002-426204P | P | 20021113 |
| | | US 2002-426282P | P | 20021113 |
| | | US 2003-460328P | P | 20030403 |
| | | US 2003-460369P | P | 20030403 |
| | | US 2003-460493P | P | 20030403 |
| | | US 2003-517915P | P | 20031107 |
| | | WO 2003-US35806 | W | 20031112 |

AB Methods of treating cancer using 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one (I) are provided. In particular, the methods are effective for the treatment of solid tumors or leukemias,

including prostate, colorectal, breast, multiple myeloma, pancreatic, small cell carcinoma, acute myelogenous leukemia, chronic myelogenous leukemia, or myelo-proliferative disease. Further provided are methods of measuring the amount of I and determining a metabolic profile therefore. The growth of both the KM12L4a and MV4;11 xenografts in mice were potently inhibited by I in vivo.

L4 ANSWER 28 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:182836 CAPLUS Full-text

DOCUMENT NUMBER: 140:235711

TITLE: Preparation of benzimidazole quinolinones for inhibiting a serine/threonine kinase

INVENTOR(S): Barsanti, Paul A.; Bussiere, Dirksen; Harrison, Stephen D.; Heise, Carla C.; Jansen, Johanna M.; Jazan, Elisa; Machajewski, Timothy D.; McBride, Christopher; McCrea, William R.; Ng, Simon; Ni, Zhi-Jie; Pecchi, Sabina; Pfister, Keith; Ramurthy, Savithri; Renhowe, Paul A.; Shafer, Cynthia M.; Silver, Joel B.; Wagman, Allan; Weismann, Marion Chiron Corporation, USA

PATENT ASSIGNEE(S): PCT Int. Appl., 570 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004018419 | A2 | 20040304 | WO 2003-US25990 | 20030819 |
| WO 2004018419 | A3 | 20040603 | | |
| WO 2004018419 | B1 | 20040729 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, WG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2496164 | A1 | 20040304 | CA 2003-2496164 | 20030819 |
| AU 2003288899 | A1 | 20040311 | AU 2003-288899 | 20030819 |
| EP 1539754 | A2 | 20050615 | EP 2003-781286 | 20030819 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003013743 | A | 20050705 | BR 2003-13743 | 20030819 |
| CN 1692112 | A | 20051102 | CN 2003-824565 | 20030819 |
| JP 2006503919 | T | 20060202 | JP 2005-501762 | 20030819 |
| IN 2005KN00484 | A | 20060106 | IN 2005-KN484 | 20050323 |
| PRIORITY APPLN. INFO.: | | | US 2002-405729P | P 20020823 |
| | | | US 2002-426107P | P 20021113 |
| | | | US 2002-426226P | P 20021113 |
| | | | US 2002-426282P | P 20021113 |
| | | | US 2002-428210P | P 20021121 |
| | | | US 2003-460327P | P 20030403 |
| | | | US 2003-460328P | P 20030403 |
| | | | US 2003-460493P | P 20030403 |

US 2003-478916P

P 20030616

US 2003-484048P

P 20030701

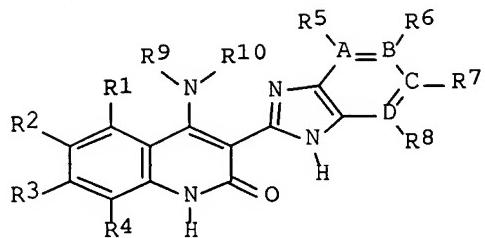
WO 2003-US25990

W 20030819

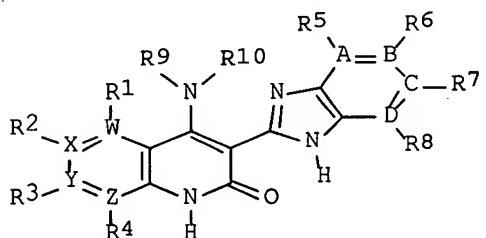
OTHER SOURCE(S) :

MARPAT 140:235711

GI



I



II

AB The title compds. [I and II; A, B, C, and D = C, N; W, X, Y and Z = C, N and at least one of W, X, Y, and Z = N; R1-R8 = H, halo, CN, NO₂, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H; or NR9R10 = 5-7 membered ring], useful for inhibiting various enzymes and treating various conditions, were prepared E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The majority of the exemplary compds. I displayed an IC₅₀ of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC₅₀ values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC₅₀ values of less than 1 μM.

L4 ANSWER 29 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:98039 CAPLUS Full-text

DOCUMENT NUMBER: 138:153534

TITLE: Preparation of benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents

INVENTOR(S): Renhowe, Paul A.; Pecchi, Sabina; Machajewski, Timothy D.; Shafer, Cynthia M.; Taylor, Clarke; McCrea, William R.; McBride, Christopher; Jazan, Elisa

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 69 pp., Cont.-in-part of U.S.
Pat. Appl. 2002 107,392.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|-------------|
| US 2003028018 | A1 | 20030206 | US 2002-116117 | 20020405 |
| US 2002107392 | A1 | 20020808 | US 2001-951265 | 20010911 |
| US 6605617 | B2 | 20030812 | | |
| EP 1650203 | A1 | 20060426 | EP 2005-17665 | 20010911 |
| R: AT, BE, CH, DE, DK, ES, FR, IE, SI, LT, LV, FI, RO, MK, | GB, GR, IT, LI, LU, NL, SE, MC, PT, CY, AL, TR | | | |
| US 2003158224 | A1 | 20030821 | US 2002-284017 | 20021030 |
| US 6774237 | B2 | 20040810 | | |
| US 2004006101 | A1 | 20040108 | US 2003-387355 | 20030312 |
| US 6762194 | B2 | 20040713 | | |
| CA 2481055 | A1 | 20031023 | CA 2003-2481055 | 20030404 |
| WO 2003087095 | A1 | 20031023 | WO 2003-US10463 | 20030404 |
| W: AE, AG, AL, AM, AT, AU, AZ, CO, CR, CU, CZ, DE, DK, DM, GM, HR, HU, ID, IL, IN, IS, LS, LT, LU, LV, MA, MD, MG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, TZ, UA, UG, US, UZ, VC, VN, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | BA, BB, BG, BR, BY, BZ, CA, CH, CN, EE, ES, FI, KP, KR, KZ, LC, LK, LR, MN, MW, MX, MZ, NI, NO, NZ, OM, TJ, TM, TN, TR, TT, ZW, AM, AZ, BY, DE, DK, EE, ES, FI, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| AU 2003226275 | A1 | 20031027 | AU 2003-226275 | 20030404 |
| EP 1497287 | A1 | 20050119 | EP 2003-746614 | 20030404 |
| R: AT, BE, CH, DE, DK, ES, FR, IE, SI, LT, LV, FI, RO, MK, | GB, GR, IT, LI, LU, NL, SE, MC, PT, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| BR 2003008996 | A | 20050222 | BR 2003-8996 | 20030404 |
| CN 1659165 | A | 20050824 | CN 2003-812909 | 20030404 |
| JP 2005527587 | T | 20050915 | JP 2003-584051 | 20030404 |
| US 2004097545 | A1 | 20040520 | US 2003-613411 | 20030703 |
| US 6800760 | B2 | 20041005 | | |
| US 2005054672 | A1 | 20050310 | US 2004-886950 | 20040708 |
| NO 2004004776 | A | 20041207 | NO 2004-4776 | 20041103 |
| US 2005209456 | A1 | 20050922 | US 2005-92137 | 20050329 |
| PRIORITY APPLN. INFO.: | | | US 2000-232159P | P 20000911 |
| | | | US 2001-951265 | A2 20010911 |
| | | | EP 2001-973722 | A3 20010911 |
| | | | US 2002-116117 | A 20020405 |
| | | | US 2002-284017 | A1 20021030 |
| | | | WO 2003-US10463 | W 20030404 |
| | | | US 2004-886950 | A1 20040708 |

OTHER SOURCE(S): MARPAT 138:153534
GI

AB Title compds. of formulas I and II are provided [for I: Z = O, S, (un)substituted NH; Y = certain OH derivs., CHO, esters and amides of CO₂H, certain NH₂ derivs.; R₁-R₄ = H, halo, cyano, NO₂, OH or derivs., NH₂ or derivs., (un)substituted amidinyl, guanidinyl, alk(en/yn)yl, aryl, heterocyclyl, CHO, CO₂H and esters and amides; R₅-R₈ = H, halo, NO₂, OH or derivs., NH₂ or derivs., SH or derivs., cyano, etc.; R₉ = H, OH, (un)substituted alkoxy or aryloxy, NH₂ or derivs., (un)substituted alkyl or aryl, CHO, alkanoyl, aroyl; for II: A, B, D, E = C or N, with at least one being N; Y = H, OH or derivs., SH or derivs., NH₂ or derivs., cyano, various acyl groups, (un)substituted alk(en/yn)yl, aralkyl, heterocycloalkyl, aryl, etc.; R₁-R₈ = H, halo, NO₂, cyano, OH or derivs., NH₂ or derivs., acyl, SH or derivs., etc.; R₉ = H, OH, (un)substituted alkoxy, aryloxy, NH₂ or derivs., aryl, CHO, alkanoyl, aroyl]. Also provided are pharmaceutical formulations including the compds. or their pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, which may be prepared by mixing the compds. or salts with a carrier and water. A disclosed method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed preps. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (preps. given), carried out in refluxing ClCH₂CH₂Cl in the presence of SnCl₄, gave the invention quinolinone III. Many compds. I and II had in vitro IC₅₀ values of less than 10 μM with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

L4 ANSWER 30 OF 50 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:220574 CAPLUS Full-text

DOCUMENT NUMBER: 136:263158

TITLE: Benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents

INVENTOR(S): Renhowe, Paul; Pecchi, Sabina; Machajewski, Tim; Shafer, Cynthia; Taylor, Clarke; McCrea, Bill; McBride, Chris; Jazan, Elisa; Wernette-Hammond, Mary-Ellen; Harris, Alex

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 207 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2002022598 | A1 | 20020321 | WO 2001-US42131 | 20010911 |
| WO 2002022598 | A8 | 20021121 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, | | | | |

US, UZ, VN, YU, ZA, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2421120 A1 20020321 CA 2001-2421120 20010911
 AU 200193275 A 20020326 AU 2001-93275 20010911
 EP 1317442 A1 20030611 EP 2001-973722 20010911
 EP 1317442 B1 20051116
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 HU 200301045 A2 20031229 HU 2003-1045 20010911
 BR 2001013757 A 20040302 BR 2001-13757 20010911
 JP 2004509112 T 20040325 JP 2002-526851 20010911
 NZ 524717 A 20040924 NZ 2001-524717 20010911
 AT 309996 T 20051215 AT 2001-973722 20010911
 ES 2250480 T3 20060416 ES 2001-1973722 20010911
 EP 1650203 A1 20060426 EP 2005-17665 20010911
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 AP 1666 A 20061031 AP 2003-2781 20010911
 W: GM, GH, KE, LS, MW, MZ, SL, SD, SZ, TZ, UG, ZM, ZW
 SG 129306 A1 20070226 SG 2005-1676 20010911
 ZA 2003001578 A 20040826 ZA 2003-1578 20030226
 IN 2003KN00244 A 20050311 IN 2003-KN244 20030226
 NO 2003001097 A 20030325 NO 2003-1097 20030310
 US 2004006101 A1 20040108 US 2003-387355 20030312
 US 6762194 B2 20040713
 BG 107709 A 20040130 BG 2003-107709 20030408
 HK 1053644 A1 20060504 HK 2003-104217 20030612
 US 2005054672 A1 20050310 US 2004-886950 20040708
 US 2005209456 A1 20050922 US 2005-92137 20050329
 AU 2005202068 A1 20050602 AU 2005-202068 20050513
 PRIORITY APPLN. INFO.: US 2000-232159P P 20000911
 AU 2001-293275 A3 20010911
 EP 2001-973722 A3 20010911
 US 2001-951265 A1 20010911
 WO 2001-US42131 W 20010911
 US 2002-284017 A1 20021030
 US 2004-886950 A1 20040708

OTHER SOURCE(S): MARPAT 136:263158
 GI

Graves
as Anc or
Cmax

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. of formulas I and II are provided [for I: Z = O, S, (un)substituted NH; Y = certain OH derivs., CHO, esters and amides of CO₂H, certain NH₂ derivs.; R1-R4 = H, halo, cyano, NO₂, OH or derivs., NH₂ or derivs., (un)substituted amidinyl, guanidinyl, alk(en/yn)yl, aryl, heterocyclyl, CHO, CO₂H and esters and amides; R5-R8 = H, halo, NO₂, OH or derivs., NH₂ or derivs., SH or derivs., cyano, etc.; R9 = H, OH, (un)substituted alkoxy or aryloxy, NH₂ or derivs., (un)substituted alkyl or aryl, CHO, alkanoyl, aroyl; for II: A, B, D, E = C or N, with at least one being N; Y = H, OH or derivs., SH or derivs., NH₂ or derivs., cyano, various acyl groups, (un)substituted alk(en/yn)yl, aralkyl, heterocycloalkyl, aryl, etc.; R1-R8 = H, halo, NO₂, cyano, OH or derivs., NH₂ or derivs., acyl, SH or derivs., etc.; R9 = H, OH, (un)substituted alkoxy, aryloxy, NH₂ or derivs., aryl, CHO, alkanoyl, aroyl]. Also provided are pharmaceutical formulations

including the compds. or their pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, which may be prepared by mixing the compds. or salts with a carrier and water. A disclosed method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed preps. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (preps. given), carried out in refluxing ClCH₂CH₂Cl in the presence of SnCl₄, gave the invention quinolinone III. Many compds. I and II had in vitro IC₅₀ values of less than 10 μM with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2007:83463 USPATFULL Full-text

TITLE: Use of tyrosine kinase inhibitor to treat diabetes

INVENTOR(S): Hagerkvist, Robert Per, Hoganasgatan 7B, Uppsala,
SWEDEN 75330
Welsh, Nils Richard, Uppsala, SWEDEN

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|-----------------------|
| PATENT INFORMATION: | US 2007072932 | A1 | 20070329 |
| APPLICATION INFO.: | US 2004-556984 | A1 | 20040526 (10) |
| | WO 2004-EP5679 | | 20040526 |
| | | | 20060622 PCT 371 date |

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | GB 2003-12086 | 20030527 |
| | GB 2004-2682 | 20040206 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | NOVARTIS, CORPORATE INTELLECTUAL PROPERTY, ONE HEALTH PLAZA 104/3, EAST HANOVER, NJ, 07936-1080, US | |
| NUMBER OF CLAIMS: | 8 | |
| EXEMPLARY CLAIM: | 1-10 | |
| NUMBER OF DRAWINGS: | 2 Drawing Page(s) | |
| LINE COUNT: | 857 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to the use of a c-Abl-, PDGF-R-, or c-kit- tyrosine kinase inhibitor, e.g. 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl)pyrimidin-2-ylamino]phenyl- benzamide, or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of diabetes, e.g. type I diabetes, type II diabetes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 32 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2007:30909 USPATFULL Full-text

TITLE: Multicyclic sulfonamide compounds as inhibitors of histone deacetylase for the treatment of disease

INVENTOR(S) :

Malecha, James W., San Diego, CA, UNITED STATES
Noble, Stewart A., San Diego, CA, UNITED STATES
Wiley, Brandon M., Philadelphia, PA, UNITED STATES
Hoffman, Timothy Z., San Diego, CA, UNITED STATES
Bonnefous, Celine, San Diego, CA, UNITED STATES
Sertic, Michael, Euclid, OH, UNITED STATES
Wash, Paul L., San Diego, CA, UNITED STATES
Smith, Nicholas D., San Diego, CA, UNITED STATES
Hassig, Christian A., Mira Mesa, CA, UNITED STATES
Scranton, Shawn A., San Diego, CA, UNITED STATES
Payne, Joseph E., Oceanside, CA, UNITED STATES
Hager, Jeffery, San Diego, CA, UNITED STATES
KALYPSYS, INC. (U.S. corporation)

PATENT ASSIGNEE(S) :

NUMBER KIND DATE

PATENT INFORMATION:

US 2007027184 A1 20070201
APPLICATION INFO.: US 2006-496784 A1 20060727 (11)

NUMBER DATE

PRIORITY INFORMATION:

US 2005-704091P 20050729 (60)
US 2006-780129P 20060307 (60)

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

INTERNATIONAL PATENT GROUP, ATTN: MS LAVERN HALL, P.O.
BOX 38129, ST. LOUIS, MO, 63138, US

NUMBER OF CLAIMS:

64

EXEMPLARY CLAIM:

1

LINE COUNT:

2549

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed herein are sulfonamide compounds of Formula VII as described herein. ##STR1## Methods and compositions are disclosed for treating disease states including, but not limited to cancers, autoimmune diseases, tissue damage, central nervous system disorders, neurodegenerative disorders, fibrosis, bone disorders, polyglutamine-repeat disorders, anemias, thalassemias, inflammatory conditions, cardiovascular conditions, and disorders in which angiogenesis play a role in pathogenesis, using the compounds of the invention. In addition, methods of modulating the activity of histone deacetylase (HDAC) are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 33 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2006:215594 USPATFULL Full-text

TITLE: Treatment of metastasized tumors

INVENTOR(S) : Menezes, Daniel Lopes De, Emeryville, CA, UNITED STATES

Heise, Carla, Benicia, CA, UNITED STATES

Xin, Xiaohua, Palo Alto, CA, UNITED STATES

PATENT ASSIGNEE(S) : Chiron Corporation (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION:

US 2006183750 A1 20060817
APPLICATION INFO.: US 2006-342257 A1 20060127 (11)

METASTASE ZERO

Tumor

No Ave. or Comp

NUMBER DATE

PRIORITY INFORMATION:

US 2005-647568P 20050127 (60)

US 2005-669245P 20050406 (60)
US 2005-722053P 20050929 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Chiron Corporation, Intellectual Property - R440, P.O.
Box 8097, Emeryville, CA, 94662-8097, US

NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 2547

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of treating metastatic cancer such as metastasized tumors include administering a compound of Structure I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, a pharmaceutically acceptable salt or the tautomer, or a mixture thereof to a subject. The compound, tautomer, salt of the compound, salt of the tautomer, or mixture thereof may be used to prepare medicaments for treating metastatic cancer. The variable A has the values defined herein. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 34 OF 50 USPATFULL on STN
ACCESSION NUMBER: 2006:159951 USPATFULL Full-text
TITLE: Use of sulfonamide-including compounds in combination with angiogenesis inhibitors
INVENTOR(S): Owa, Takashi, Tsukuba-shi, JAPAN
Ozawa, Yoichi, Tsukuba-shi, JAPAN
Semba, Taro, Tsukuba-shi, JAPAN
PATENT ASSIGNEE(S): Eisai Co., Ltd., Tokyo, JAPAN (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2006135486 | A1 | 20060622 |
| APPLICATION INFO.: | US 2005-226655 | A1 | 20050913 (11) |

| | NUMBER | DATE |
|-----------------------|-----------------|---------------|
| PRIORITY INFORMATION: | JP 2005-54150 | 20050228 |
| | JP 2005-54475 | 20050228 |
| | US 2004-609452P | 20040913 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DARBY & DARBY P.C., P. O. BOX 5257, NEW YORK, NY,
10150-5257, US

NUMBER OF CLAIMS: 52
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 3301

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to pharmaceutical compositions comprising a sulfonamide-including compound in combination with an angiogenesis inhibitor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 35 OF 50 USPATFULL on STN
ACCESSION NUMBER: 2005:299638 USPATFULL Full-text
TITLE: Inhibition of FGFR3 and treatment of multiple myeloma

INVENTOR(S) : Cai, Shaopei, Seattle, WA, UNITED STATES
 Chou, Joyce, El Cerrito, CA, UNITED STATES
 Harwood, Eric, Seattle, WA, UNITED STATES
 Heise, Carla C., Benicia, CA, UNITED STATES
 Machajewski, Timothy D., Martinez, CA, UNITED STATES
 Ryckman, David, Bellevue, WA, UNITED STATES
 Shang, Xiao, Bellevue, WA, UNITED STATES
 Wiesmann, Marion, Brisbane, CA, UNITED STATES
 Zhu, Shuguang, Shoreline, WA, UNITED STATES
 Chiron Corporation (U.S. corporation)

PATENT ASSIGNEE(S) :

PATENT INFORMATION:

APPLICATION INFO.:

RELATED APPLN. INFO.:

| NUMBER | KIND | DATE | |
|--|------|---------------|------------------|
| US 2005261307 | A1 | 20051124 | <i>Inhibitor</i> |
| US 2004-983174 | A1 | 20041105 (10) | <i>fGF3</i> |
| Continuation-in-part of Ser. No. US 2003-644055, filed | | | |
| on 19 Aug 2003, PENDING | | | |

No Ance or Cross

PRIORITY INFORMATION:

| NUMBER | DATE |
|-----------------|---------------|
| US 2003-517915P | 20031107 (60) |
| US 2003-526426P | 20031202 (60) |
| US 2003-526425P | 20031202 (60) |
| US 2004-546017P | 20040219 (60) |
| US 2002-405729P | 20020823 (60) |
| US 2002-426107P | 20021113 (60) |
| US 2002-426226P | 20021113 (60) |
| US 2002-426282P | 20021113 (60) |
| US 2002-428210P | 20021121 (60) |
| US 2003-460328P | 20030403 (60) |
| US 2003-460493P | 20030403 (60) |
| US 2003-460327P | 20030403 (60) |
| US 2003-478916P | 20030616 (60) |
| US 2003-484048P | 20030701 (60) |

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE: Chiron Corporation, Intellectual Property - R440, P.O.
 Box 8097, Emeryville, CA, 94662-8097, US

NUMBER OF CLAIMS: 28

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 34 Drawing Page(s)

LINE COUNT: 17221

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of inhibiting fibroblast growth factor receptor 3 and treating various conditions mediated by fibroblast growth factor receptor 3 are provided that include administering to a subject a compound of Structure I, a pharmaceutically acceptable salt thereof, a tautomer thereof, or a pharmaceutically acceptable salt of the tautomer. Compounds having the Structure I have the following structure where and have the variables described herein. Such compounds may be used to prepare medicaments for use in inhibiting fibroblast growth factor receptor 3 and for use in treating conditions mediated by fibroblast growth factor receptor 3 such as multiple myeloma. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 36 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2005:293608 USPATFULL Full-text

TITLE: Combination therapy with CHK1 inhibitors

INVENTOR(S) : Gesner, Thomas G., Kensington, CA, UNITED STATES
Barsanti, Paul A., Pleasant Hill, CA, UNITED STATES
Harrison, Stephen D., Albany, CA, UNITED STATES
Ni, Zhi-Jie, Fremont, CA, UNITED STATES
Brammeier, Nathan M., Walnut Creek, CA, UNITED STATES
Zhou, Yasheen, Moraga, CA, UNITED STATES
Le, Vincent P., San Francisco, CA, UNITED STATES
CHIRON CORPORATION (U.S. corporation)

PATENT ASSIGNEE(S) :

PATENT INFORMATION:

APPLICATION INFO.:

RELATED APPLN. INFO.:

| NUMBER | KIND | DATE |
|---|------|---------------|
| US 2005256157 | A1 | 20051117 |
| US 2005-41191 | A1 | 20050121 (11) |
| Continuation-in-part of Ser. No. US 2003-644055, filed
on 19 Aug 2003, PENDING | | |

PRIORITY INFORMATION:

| NUMBER | DATE |
|-----------------|---------------|
| US 2004-538984P | 20040123 (60) |
| US 2002-405729P | 20020823 (60) |
| US 2002-426282P | 20021113 (60) |
| US 2002-426107P | 20021113 (60) |
| US 2002-426226P | 20021113 (60) |
| US 2002-428210P | 20021121 (60) |
| US 2003-460493P | 20030403 (60) |
| US 2003-460328P | 20030403 (60) |
| US 2003-460327P | 20030403 (60) |
| US 2003-478916P | 20030616 (60) |
| US 2003-484048P | 20030701 (60) |

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

Chiron Corporation, Intellectual Property - R440, P.O.
Box 8097, Emeryville, CA, 94662-8097, US

NUMBER OF CLAIMS:

32

EXEMPLARY CLAIM:

1

NUMBER OF DRAWINGS:

28 Drawing Page(s)

LINE COUNT:

16679

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of Structure I, and salts, tautomers, stereoisomers, and mixtures thereof may be used in methods of inhibiting checkpoint kinase 1 in subjects, in methods for inducing cell cycle progression, and in methods for increasing apoptosis in cells. Such compounds may be used to prepare pharmaceutical compositions and may be used in conjunction with DNA damaging agents. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 37 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2005:275261 USPATFULL Full-text

TITLE: Modulation of inflammatory and metastatic processes

INVENTOR(S): Heise, Carla, Benicia, CA, UNITED STATES

Lee, Sang H., Waltham, MA, UNITED STATES

PATENT ASSIGNEE(S): Chiron Corporation (U.S. corporation)

| NUMBER | KIND | DATE |
|---------------|------|---------------|
| US 2005239825 | A1 | 20051027 |
| US 2005-61386 | A1 | 20050218 (11) |

PATENT INFORMATION:

APPLICATION INFO.:

| | NUMBER | DATE |
|-----------------------|--|---|
| PRIORITY INFORMATION: | US 2004-546395P
US 2004-547103P
US 2004-554771P | 20040220 (60)
20040223 (60)
20040319 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | Chiron Corporation, Intellectual Property - R440, P.O.
Box 8097, Emeryville, CA, 94662-8097, US | |
| NUMBER OF CLAIMS: | 39 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 9 Drawing Page(s) | |
| LINE COUNT: | 5172 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of using compounds having Structure I or the salts or tautomers of the compounds in the treatment of disorders relating to cell adhesion and metastatic processes are presented herein. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 38 OF 50 USPATFULL on STN
 ACCESSION NUMBER: 2005:241451 USPATFULL Full-text
 TITLE: Quinolinone derivatives
 INVENTOR(S): Renhowe, Paul A., Danville, CA, UNITED STATES
 Shafer, Cynthia M., Moraga, CA, UNITED STATES
 Machajewski, Timothy D., Martinez, CA, UNITED STATES
 Pecchi, Sabina, Oakland, CA, UNITED STATES
 McBride, Christopher, Oakland, CA, UNITED STATES
 PATENT ASSIGNEE(S): Chiron Corporation (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2005209456 | A1 | 20050922 |
| APPLICATION INFO.: | US 2005-92137 | A1 | 20050329 (11) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 2004-886950, filed on 8 Jul 2004, PENDING Continuation of Ser. No. US 2002-284017, filed on 30 Oct 2002, GRANTED, Pat. No. US 6774237
Continuation of Ser. No. US 2001-951265, filed on 11 Sep 2001, GRANTED, Pat. No. US 6605617 | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2000-232159P | 20000911 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | Chiron Corporation, Intellectual Property - R440, P.O.
Box 8097, Emeryville, CA, 94662-8097, US | |
| NUMBER OF CLAIMS: | 14 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 5434 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for synthesizing a 4-amino substituted quinolinone includes reacting a substituted or unsubstituted 2-benzimidazolyl-2-acetate with a substituted or unsubstituted 2-aminobenzonitrile in the presence of a base or an acid. A 4-amino substituted quinolinone compound is formed by the reaction, and the 4-amino substituted quinolinone compound comprises a benzimidazole group.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 39 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2005:241242 USPATFULL Full-text

TITLE: Pharmaceutically acceptable salts of quinolinone compounds having improved pharmaceutical properties

INVENTOR(S): Cai, Shaopei, Seattle, WA, UNITED STATES
Chou, Joyce, El Cerrito, CA, UNITED STATES
Harwood, Eric, Seattle, WA, UNITED STATES
Machajewski, Timothy, Martinez, CA, UNITED STATES
Ryckman, David, Bellevue, WA, UNITED STATES
Shang, Xiao, Bellevue, WA, UNITED STATES
Zhu, Shuguang, Shoreline, WA, UNITED STATES
Okhamafe, Augustus O., Concord, CA, UNITED STATES
Tesconi, Marc S., Monroe, NY, UNITED STATES
PATENT ASSIGNEE(S): Chiron Corporation (U.S. corporation)

| | NUMBER | KIND | DATE | |
|--|--|---------------|---------------|----------------|
| PATENT INFORMATION: | US 2005209247 | A1 | 20050922 | TREATING VEGF |
| APPLICATION INFO.: | US 2004 982543 | A1 | 20041105 (10) | NO ANC or Cmax |
| | NUMBER | DATE | | |
| PRIORITY INFORMATION: | US 2003-517915P | 20031107 (60) | | |
| | US 2003-526425P | 20031202 (60) | | |
| | US 2003-526426P | 20031202 (60) | | |
| | US 2004-546017P | 20040219 (60) | | |
| DOCUMENT TYPE: | Utility | | | |
| FILE SEGMENT: | APPLICATION | | | |
| LEGAL REPRESENTATIVE: | Chiron Corporation, Intellectual Property - R440, P.O. Box 8097, Emeryville, CA, 94662-8097, US | | | |
| NUMBER OF CLAIMS: | 45 | | | |
| EXEMPLARY CLAIM: | 1 | | | |
| NUMBER OF DRAWINGS: | 18 Drawing Page(s) | | | |
| LINE COUNT: | 7116 | | | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | | | |
| AB | A lacate salt of a compound of Formula I or a tautomer of the compound, wherein Formula I has the following structure and R. ¹ -R. ⁹ and R. ¹² -R. ¹⁴ are as defined herein ##STR1## | | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 40 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2005:234162 USPATFULL Full-text

TITLE: Benzimidazole quinolinones and uses thereof

INVENTOR(S): Barsanti, Paul A., Pleasant Hill, CA, UNITED STATES
Bussiere, Dirksen, San Leandro, CA, UNITED STATES
Harrison, Stephen D., Albany, CA, UNITED STATES
Heise, Carla C., Benicia, CA, UNITED STATES
Jansen, Johanna M., San Francisco, CA, UNITED STATES
Jazan, Elisa, Berkeley, CA, UNITED STATES
Machajewski, Timothy D., Martinez, CA, UNITED STATES
McBride, Christopher, Oakland, CA, UNITED STATES
McCrea, William R. JR., Berkeley, CA, UNITED STATES
Ng, Simon, Walnut Creek, CA, UNITED STATES
Ni, Zhi-Jie, Fremont, CA, UNITED STATES
Pecchi, Sabina, Oakland, CA, UNITED STATES
Pfister, Keith B., San Ramon, CA, UNITED STATES

| | NUMBER | KIND | DATE |
|--|---|---------------|---------------|
| PATENT INFORMATION: | US 2005137399 | A1 | 20050623 |
| APPLICATION INFO.: | US 2004-982757 | A1 | 20041105 (10) |
| | NUMBER | DATE | |
| PRIORITY INFORMATION: | US 2003-517915P | 20031107 (60) | |
| | US 2003-526425P | 20031202 (60) | |
| | US 2003-526426P | 20031202 (60) | |
| | US 2004-546017P | 20040219 (60) | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | Chiron Corporation, Intellectual Property - R440, P.O. Box 8097, Emeryville, CA, 94662-8097, US | | |
| NUMBER OF CLAIMS: | 71 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 2006 | | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | | |
| AB | A method of synthesizing a substituted or unsubstituted 4-amino-3-benzimidazolyl quinolinone compound includes reacting a first compound having the formula I with a second compound having the formula II in a suitable solvent in the presence of a sodium or potassium salt of a base. The first compound and the second compound have the following structures where the variables have the values described herein: ##STR1## | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

| | | |
|---------------------|--|--------|
| L4 ANSWER 42 OF 50 | USPATFULL | on STN |
| ACCESSION NUMBER: | 2005:63630 USPATFULL <u>Full-text</u> | |
| TITLE: | Quinolinone derivatives | |
| INVENTOR(S): | Renhowe, Paul A., Danville, CA, UNITED STATES | |
| | Pecchi, Sabina, Oakland, CA, UNITED STATES | |
| | Machajewski, Timothy D., Martinez, CA, UNITED STATES | |
| | Shafer, Cynthia M., El Sobrante, CA, UNITED STATES | |
| | Taylor, Clarke, Albany, CA, UNITED STATES | |
| | McCREA, William R., Berkeley, CA, UNITED STATES | |
| | McBride, Christopher, Oakland, CA, UNITED STATES | |
| | Jazan, Elisa, Richmond, CA, UNITED STATES | |
| PATENT ASSIGNEE(S): | Chiron Corporation (U.S. corporation) | |

| | | | |
|-----------------------|---|------|---------------|
| PATENT INFORMATION: | NUMBER | KIND | DATE |
| | US 2005054672 | A1 | 20050310 |
| APPLICATION INFO.: | US 2004-886950 | A1 | 20040708 (10) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 2002-284017, filed on 30 Oct 2002, GRANTED, Pat. No. US 6774237 Continuation of Ser. No. US 2001-951265, filed on 11 Sep 2001, GRANTED, Pat. No. US 6605617 | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2000-232159P | 20000911 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | Young J. Suh, Chiron Corporation, P.O. Box 8097, Emeryville, CA, 94662 | |
| NUMBER OF CLAIMS: | 16 | |

EXEMPLARY CLAIM: 1
LINE COUNT: 5757

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Organic compounds having the formula I are provided where the variables have the values described herein. ##STR1##

Pharmaceutical formulations include the organic compounds or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier and may be prepared by mixing the organic compounds or pharmaceutically acceptable salts of the organic compounds with a carrier and water. A method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient in need thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 43 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2005:44347 USPATFULL Full-text
TITLE: Fluoro substituted omega-carboxyaryl diphenyl urea for
the treatment and prevention of diseases and conditions
INVENTOR(S): Boyer, Stephen, Hilden, GERMANY, FEDERAL REPUBLIC OF
Dumas, Jacques, Bethany, CT, UNITED STATES
Riedl, Bernd, Wuppertal, GERMANY, FEDERAL REPUBLIC OF
Wilhelm, Scott, Orange, CT, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2005038080 | A1 | 20050217 |
| APPLICATION INFO.: | US 2004-895985 | A1 | 20040722 (10) |

| | NUMBER | DATE |
|-----------------------|-----------------|---------------|
| PRIORITY INFORMATION: | US 2003-489102P | 20030723 (60) |
| | US 2004-540326P | 20040202 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON
BLVD., SUITE 1400, ARLINGTON, VA, 22201

NUMBER OF CLAIMS: 54

EXEMPLARY CLAIM: 1

LINE COUNT: 2492

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound of Formula (I): ##STR1##

salts thereof, prodrugs thereof, metabolites thereof, pharmaceutical compositions containing such a compound, and use of such compound and compositions to treat diseases mediated by raf, VEGFR, PDGFR, p38 and flt-3.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 44 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2004:280895 USPATFULL Full-text
TITLE: Methods of treating cancer and related methods
INVENTOR(S): Hannah, Alison, Sebastopol, CA, UNITED STATES
Harwood, Eric, Seattle, WA, UNITED STATES
Haroldsen, Peter, Pacifica, CA, UNITED STATES

PATENT ASSIGNEE(S) :

Heise, Carla, Benicia, CA, UNITED STATES
 Machajewski, Timothy, Martinez, CA, UNITED STATES
 Samara, Emil, Danville, CA, UNITED STATES
 Shang, Xiao, Bellevue, WA, UNITED STATES
 Vora, Jayesh, Martinez, CA, UNITED STATES
 Zhu, Shuguang, Seattle, WA, UNITED STATES
 Chiron Corporation (U.S. corporation)

| | NUMBER | KIND | DATE | |
|---------------------|----------------|------|---------------|--------------------|
| PATENT INFORMATION: | US 2004220196 | A1 | 20041104 | <i>APPLICATION</i> |
| APPLICATION INFO.: | US 2003-706328 | A1 | 20031112 (10) | |

| | NUMBER | DATE |
|-----------------------|-----------------|---------------|
| PRIORITY INFORMATION: | US 2003-460369P | 20030403 (60) |
| | US 2003-460493P | 20030403 (60) |
| | US 2003-460328P | 20030403 (60) |
| | US 2002-426204P | 20021113 (60) |
| | US 2002-426282P | 20021113 (60) |
| | US 2002-426107P | 20021113 (60) |
| | US 2003-517915P | 20031107 (60) |

DOCUMENT TYPE: Utility
 FILE SEGMENT: APPLICATION
 LEGAL REPRESENTATIVE: Chiron Corporation, Intellectual Property - R440, P.O.
 Box 8097, Emeryville, CA, 94662-8097

NUMBER OF CLAIMS: 58

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 2 Drawing Page(s)

LINE COUNT: 2045

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of treating cancer using 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one are provided. In particular, the methods are effective for the treatment of solid tumors or leukemias, including prostate, colorectal, breast, multiple myeloma, pancreatic, small cell carcinoma, acute myelogenous leukemia, chronic myelogenous leukemia, or myelo-proliferative disease. Further provided are methods of measuring the amount of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one and determining a metabolic profile therefore.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 45 OF 50 USPATFULL on STN
 ACCESSION NUMBER: 2004:127561 USPATFULL Full-text
 TITLE: Quinolinone derivatives
 INVENTOR(S): Renhowe, Paul A., Danville, CA, UNITED STATES
 Pecchi, Sabina, Oakland, CA, UNITED STATES
 Machajewski, Timothy D., Martinez, CA, UNITED STATES
 Shafer, Cynthia M., El Sobrante, CA, UNITED STATES
 Taylor, Clarke, Ann Arbor, MI, UNITED STATES
 McCrea, William R., JR., Berkeley, CA, UNITED STATES
 McBride, Christopher, Oakland, CA, UNITED STATES
 Jazan, Elisa, Richmond, CA, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2004097545 | A1 | 20040520 |
| APPLICATION INFO.: | US 6800760 | B2 | 20041005 |
| | US 2003-613411 | A1 | 20030703 (10) |

✓ METHOD USING
 GENUS - GENUS
 DOES NOT ENCOMPASS
 COMPOUND. NO
 ANC OR CROZ

RELATED APPLN. INFO.: Division of Ser. No. US 2001-951265, filed on 11 Sep 2001, GRANTED, Pat. No. US 6605617

NUMBER DATE

PRIORITY INFORMATION: US 2000-232159P 20000911 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Chiron Corporation, Intellectual Property, P.O. Box 8097, Emeryville, CA, 94662-8097
NUMBER OF CLAIMS: 37
EXEMPLARY CLAIM: 1
LINE COUNT: 6582

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Organic compounds having the formulas I and II are provided where the variables have the values described herein. ##STR1##

Pharmaceutical formulations include the organic compounds or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier and may be prepared by mixing the organic compounds or pharmaceutically acceptable salts of the organic compounds with a carrier and water. A method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient in need thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 46 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2004:121119 USPATFULL Full-text
TITLE: Benzimidazole quinolinones and uses thereof
INVENTOR(S): Barsanti, Paul A., Walnut Creek, CA, UNITED STATES
Bussiere, Dirksen, San Leandro, CA, UNITED STATES
Harrison, Stephen D., Albany, CA, UNITED STATES
Heise, Carla C., Benicia, CA, UNITED STATES
Jansen, Johanna M., San Francisco, CA, UNITED STATES
Jazan, Elisa, Richmond, CA, UNITED STATES
Michajewski, Timothy D., Martinez, CA, UNITED STATES
McBride, Christopher, Oakland, CA, UNITED STATES
McCrea, William R., JR., Berkeley, CA, UNITED STATES
Ng, Simon, Walnut Creek, CA, UNITED STATES
Ni, Zhi-Jie, Fremont, CA, UNITED STATES
Pecchi, Sabina, Oakland, CA, UNITED STATES
Pfister, Keith B., San Ramon, CA, UNITED STATES
Ramurthy, Savithri, Walnut Creek, CA, UNITED STATES
Renhowe, Paul A., Danville, CA, UNITED STATES
Shafer, Cynthia M., El Sobrante, CA, UNITED STATES
Silver, Joel B., Concord, NH, UNITED STATES
Wagman, Allan S., Belmont, CA, UNITED STATES
Wiesmann, Marion, Brisbane, CA, UNITED STATES
PATENT ASSIGNEE(S): Chiron Corporation (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2004092535 A1 20040513
APPLICATION INFO.: US 2003644055 A1 20030819 (10) *Supra 1*

NUMBER DATE

PRIORITY INFORMATION: US 2002-405729P 20020823 (60)
US 2002-426107P 20021113 (60)
US 2002-426226P 20021113 (60)
US 2002-426282P 20021113 (60)
US 2002-428210P 20021121 (60)
US 2003-460328P 20030403 (60)
US 2003-460493P 20030403 (60)
US 2003-460327P 20030403 (60)
US 2003-478916P 20030616 (60)
US 2003-484048P 20030701 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Chiron Corporation, Intellectual Property - R440, P.O.
Box 8097, Emeryville, CA, 94662-8097

NUMBER OF CLAIMS: 68

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 14 Drawing Page(s)

LINE COUNT: 18050

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of inhibiting various enzymes and treating various conditions are provided that include administering to a subject a compound of Structure I or IB, a pharmaceutically acceptable salt thereof, a tautomer thereof, or a pharmaceutically acceptable salt of the tautomer. Compounds having the Structure I and IB have the following structures and have the variables described herein. Such compounds may be used to prepare medicaments for use in inhibiting various enzymes and for use in treating conditions mediated by such enzymes. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 47 OF 50 USPATFULL on STN

ACCESSION NUMBER: 2004:7861 USPATFULL Full-text

TITLE: Quinolinone derivatives

INVENTOR(S): Renhowe, Paul A., Danville, CA, UNITED STATES
Pecchi, Sabina, Oakland, CA, UNITED STATES
Machajewski, Timothy D., Martinez, CA, UNITED STATES
Shafer, Cynthia M., El Sobrante, CA, UNITED STATES
Taylor, Clarke, Ann Arbor, MI, UNITED STATES
McCREA, William R., JR., Berkeley, CA, UNITED STATES
McBride, Christopher, Oakland, CA, UNITED STATES
Jazan, Eliza, Richmond, CA, UNITED STATES

PATENT ASSIGNEE(S): CHIRON CORPORATION (U.S. corporation)

| | NUMBER | KIND | DATE | |
|-----------------------|--|------|---------------|----------------------|
| PATENT INFORMATION: | US 2004006101 | A1 | 20040108 | ✓ <i>Compounds?</i> |
| | US 6762194 | B2 | 20040713 | <i>composition -</i> |
| APPLICATION INFO.: | US 2003-387355 | A1 | 20030312 (10) | <i>no methods</i> |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 2002-284017, filed on 30 Oct 2002, PENDING Continuation of Ser. No. US 2001-951265, filed on 11 Sep 2001, GRANTED, Pat. No. US 6605617 | | | |

| | NUMBER | DATE |
|-----------------------|---|---------------|
| PRIORITY INFORMATION: | US 2000-232159P | 20000911 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | Steven W. Collier, Chiron Corporation, P.O. Box 8097, | |

Emeryville, CA, 94662

NUMBER OF CLAIMS: 42
EXEMPLARY CLAIM: 1
LINE COUNT: 5740

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Organic compounds having the formulas I and II are provided where the variables have the values described herein. ##STR1##

Pharmaceutical formulations include the organic compounds or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier and may be prepared by mixing the organic compounds or pharmaceutically acceptable salts of the organic compounds with a carrier and water. A method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient in need thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 48 OF 50 USPATFULL on STN
ACCESSION NUMBER: 2003:226411 USPATFULL Full-text
TITLE: Quinolinone derivatives
INVENTOR(S): Renhowe, Paul A., Danville, CA, UNITED STATES
Pecchi, Sabina, Oakland, CA, UNITED STATES
Machajewski, Timothy D., Martinez, CA, UNITED STATES
Shafer, Cynthia M., El Sobrante, CA, UNITED STATES
Taylor, Clarke, Ann Arbor, MI, UNITED STATES
McCrea Jr, William R., Berkeley, CA, UNITED STATES
McBride, Christopher, Oakland, CA, UNITED STATES
Jazan, Elisa, Richmond, CA, UNITED STATES
PATENT ASSIGNEE(S): Chiron Corporation (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|----------------|------|---|
| PATENT INFORMATION: | US 2003158224 | A1 | 20030821 |
| APPLICATION INFO.: | US 6774237 | B2 | 20040810 |
| RELATED APPLN. INFO.: | US 2002-284017 | A1 | 20021030 (10)
Continuation of Ser. No. US 2001-951265, filed on 11 Sep 2001, PENDING |

✓ Compounds &
Compositions -
no methods

| | NUMBER | DATE |
|-----------------------|---|---------------|
| PRIORITY INFORMATION: | US 2000-232159P | 20000911 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | Steven W. Collier, Chiron Corporation, P.O. Box 8097, Emeryville, CA, 94662 | |

NUMBER OF CLAIMS: 43

EXEMPLARY CLAIM: 1

LINE COUNT: 5881

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Organic compounds having the formulas I and II are provided where the variables have the values described herein. ##STR1##

Pharmaceutical formulations include the organic compounds or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier and may be prepared by mixing the organic compounds or pharmaceutically acceptable salts of the organic compounds with a carrier

and water. A method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient in need thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 49 OF 50 USPATFULL on STN
ACCESSION NUMBER: 2003:38371 USPATFULL Full-text
TITLE: Quinolinone derivatives
INVENTOR(S): Renhowe, Paul A., Danville, CA, UNITED STATES
Pecchi, Sabina, Oakland, CA, UNITED STATES
Machajewski, Timothy D., Martinez, CA, UNITED STATES
Shafer, Cynthia M., El Sobrante, CA, UNITED STATES
Taylor, Clarke, Ann Arbor, MI, UNITED STATES
McCrea, William R., JR., Berkeley, CA, UNITED STATES
McBride, Christopher, Oakland, CA, UNITED STATES
Jazan, Elisa, Richmond, CA, UNITED STATES
PATENT ASSIGNEE(S): Chiron Corporation (U.S. corporation)

| | NUMBER | KIND | DATE | |
|-----------------------|---|------|---------------|---------------------------------------|
| PATENT INFORMATION: | US 2003028018 | A1 | 20030206 | <i>Cancer Indexer</i> |
| APPLICATION INFO.: | US 2002-116117 | A1 | 20020405 (10) | <i>Treatment kinase w/
Genus.</i> |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 2001-951265, filed
on 11 Sep 2001, PENDING | | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2000-232159P | 20000911 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | Chiron Corporation, Intellectual Property Law Dept., PO
Box 8097, Emeryville, CA, 94662 | |
| NUMBER OF CLAIMS: | 37 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 6573 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Organic compounds having the formulas I and II are provided where the variables have the values described herein. ##STR1##

Pharmaceutical formulations include the organic compounds or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier and may be prepared by mixing the organic compounds or pharmaceutically acceptable salts of the organic compounds with a carrier and water. A method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient in need thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 50 OF 50 USPATFULL on STN
ACCESSION NUMBER: 2002:199281 USPATFULL Full-text
TITLE: Quinolinone derivatives
INVENTOR(S): Renhowe, Paul A., Danville, CA, UNITED STATES
Pecchi, Sabina, Oakland, CA, UNITED STATES
Machajewski, Timothy D., Martinez, CA, UNITED STATES
Shafer, Cynthia M., El Sobrante, CA, UNITED STATES

Taylor, Clarke, Ann Arbor, MI, UNITED STATES
 McCrea, William R., JR., Berkeley, CA, UNITED STATES
 McBride, Christopher, Oakland, CA, UNITED STATES
 Jazan, Elisa, Richmond, CA, UNITED STATES

PATENT INFORMATION:

| NUMBER | KIND | DATE |
|----------------|------|--------------|
| US 2002107392 | A1 | 20020808 |
| US 6605617 | B2 | 20030812 |
| US 2001-951265 | A1 | 20010911 (9) |

APPLICATION INFO.:

| NUMBER | DATE |
|-----------------|---------------|
| US 2000-232159P | 20000911 (60) |

PRIORITY INFORMATION:

US 2000-232159P 20000911 (60)

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

David Lentini, CHIRON CORPORATION, 4560 Horton Street,
 Emeryville, CA, 94608-2916

NUMBER OF CLAIMS:

37

EXEMPLARY CLAIM:

1

LINE COUNT:

6588

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Organic compounds having the formulas I and II are provided where the variables have the values described herein. ##STR1##

Pharmaceutical formulations include the organic compounds or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier and may be prepared by mixing the organic compounds or pharmaceutically acceptable salts of the organic compounds with a carrier and water. A method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient in need thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s 14 and "AUC"

L5 2 L4 AND "AUC"

=> d 15 1-2 ibib, abs, hitstr

L5 ANSWER 1 OF 2 USPATFULL on STN

ACCESSION NUMBER: 2005:299638 USPATFULL Full-text

TITLE: Inhibition of FGFR3 and treatment of multiple myeloma

INVENTOR(S): Cai, Shaopei, Seattle, WA, UNITED STATES

Chou, Joyce, El Cerrito, CA, UNITED STATES

Harwood, Eric, Seattle, WA, UNITED STATES

Heise, Carla C., Benicia, CA, UNITED STATES

Machajewski, Timothy D., Martinez, CA, UNITED STATES

Ryckman, David, Bellevue, WA, UNITED STATES

Shang, Xiao, Bellevue, WA, UNITED STATES

Wiesmann, Marion, Brisbane, CA, UNITED STATES

Zhu, Shuguang, Shoreline, WA, UNITED STATES

PATENT ASSIGNEE(S): Chiron Corporation (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2005261307 A1 20051124

✓ CLAIM 30 -
 TREATING PATIENTS IN
 NEED OF VEGF THERAPY
 USING CASUAL INCORPORATION
 INSTANT COMPOUND NO AUC
 OR Casax

*MULTIPLE myeloma
no Auc or Cross*

APPLICATION INFO.: US 2004-983174 A1 20041105 (10)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-644055, filed
on 19 Aug 2003, PENDING

| PRIORITY INFORMATION: | NUMBER | DATE |
|-----------------------|-----------------|---------------|
| | US 2003-517915P | 20031107 (60) |
| | US 2003-526426P | 20031202 (60) |
| | US 2003-526425P | 20031202 (60) |
| | US 2004-546017P | 20040219 (60) |
| | US 2002-405729P | 20020823 (60) |
| | US 2002-426107P | 20021113 (60) |
| | US 2002-426226P | 20021113 (60) |
| | US 2002-426282P | 20021113 (60) |
| | US 2002-428210P | 20021121 (60) |
| | US 2003-460328P | 20030403 (60) |
| | US 2003-460493P | 20030403 (60) |
| | US 2003-460327P | 20030403 (60) |
| | US 2003-478916P | 20030616 (60) |
| | US 2003-484048P | 20030701 (60) |

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Chiron Corporation, Intellectual Property - R440, P.O.
Box 8097, Emeryville, CA, 94662-8097, US

NUMBER OF CLAIMS: 28

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 34 Drawing Page(s)

LINE COUNT: 17221

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

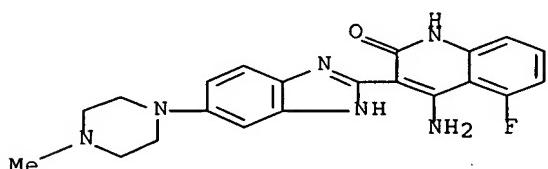
AB Methods of inhibiting fibroblast growth factor receptor 3 and treating various conditions mediated by fibroblast growth factor receptor 3 are provided that include administering to a subject a compound of Structure I, a pharmaceutically acceptable salt thereof, a tautomer thereof, or a pharmaceutically acceptable salt of the tautomer. Compounds having the Structure I have the following structure where and have the variables described herein. Such compounds may be used to prepare medicaments for use in inhibiting fibroblast growth factor receptor 3 and for use in treating conditions mediated by fibroblast growth factor receptor 3 such as multiple myeloma. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 405169-16-6P
(preparation of benzimidazole quinolinones for inhibiting FGFR3 and
treating
multiple myeloma)

RN 405169-16-6 USPATFULL

CN 2(1H)-Quinolinone, 4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-
benzimidazol-2-yl]-(CA INDEX NAME)



L5 ANSWER 2 OF 2 USPATFULL on STN

ACCESSION NUMBER: 2004:280895 USPATFULL Full-text

TITLE: Methods of treating cancer and related methods

INVENTOR(S): Hannah, Alison, Sebastopol, CA, UNITED STATES

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| NUMBER | KIND | DATE |
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Application

PRIORITY INFORMATION:

| NUMBER | DATE |
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APPLICATION

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NUMBER OF CLAIMS:

58

EXEMPLARY CLAIM:

1

NUMBER OF DRAWINGS:

2 Drawing Page(s)

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of treating cancer using 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one are provided. In particular, the methods are effective for the treatment of solid tumors or leukemias, including prostate, colorectal, breast, multiple myeloma, pancreatic, small cell carcinoma, acute myelogenous leukemia, chronic myelogenous leukemia, or myelo-proliferative disease. Further provided are methods of measuring the amount of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one and determining a metabolic profile therefore.

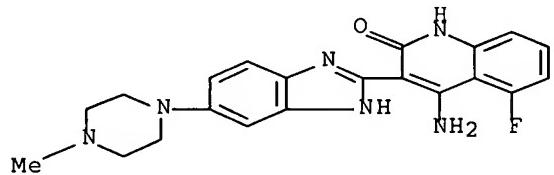
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 405169-16-6P

(preparation of benzimidazole quinolinones for inhibiting a serine/threonine kinase)

RN 405169-16-6 USPATFULL

CN 2(1H)-Quinolinone, 4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]- (CA INDEX NAME)



=> s 14 and ("tyrosine kinase")
L6 37 L4 AND ("TYROSINE KINASE")

=> s 14 and ("cancer" or "tumor")
L7 32 L4 AND ("CANCER" OR "TUMOR")

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(FILE 'HOME' ENTERED AT 11:33:03 ON 03 MAY 2007)

FILE 'REGISTRY' ENTERED AT 11:33:15 ON 03 MAY 2007
L1 STRUCTURE uploaded
L2 0 S L1 EXA
L3 2 S L1 EXA FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 11:34:23 ON 03 MAY 2007
L4 50 S L3
L5 2 S L4 AND "AUC"
L6 37 S L4 AND ("TYROSINE KINASE")
L7 32 S L4 AND ("CANCER" OR "TUMOR")

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Executing the logoff script...

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